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(FILE 'HOME' ENTERED AT 12:08:31 ON 28 FEB 2006)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
LIFESCI' ENTERED AT 12:09:07 ON 28 FEB 2006

L1 7010 S TESTIS (W) SPECIFIC
L2 431 S TYROSINE (W)LIGASE?
L3 3 S L1 AND L2
L4 2 DUP REM L3 (1 DUPLICATE REMOVED)
L5 405 S TUBULIN (A) L2
L6 7556238 S CLON? OR EXPRESS? OR RECOMBINANT
L7 83 S L5 AND L6
L8 39 DUP REM L7 (44 DUPLICATES REMOVED)
L9 8 S L8 AND TESTIS
 E FEDER J N/AU
L10 185 S E3
 E WU S/AU
L11 3568 S E3
 E NELSON T C/AU
L12 130 S E3
L13 3853 S L10 OR L11 OR L12
L14 1 S L2 AND L13

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NEWS 8 DEC 23 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
USPAT2
NEWS 9 JAN 13 IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 10 JAN 13 New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
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NEWS 11 JAN 17 Pre-1988 INPI data added to MARPAT
NEWS 12 JAN 17 IPC 8 in the WPI family of databases including WPIFV
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added to TULSA
NEWS 15 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist
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NEWS 16 FEB 22 Status of current WO (PCT) information on STN
NEWS 17 FEB 22 The IPC thesaurus added to additional patent databases on STN
NEWS 18 FEB 22 Updates in EPFULL; IPC 8 enhancements added
NEWS 19 FEB 27 New STN AnaVist pricing effective March 1, 2006

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CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
<http://download.cas.org/express/v8.0-Discover/>

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=> s testis (w) specific
L1 7010 TESTIS (W) SPECIFIC

=> s tyrosine (w) ligase?
L2 431 TYROSINE (W) LIGASE?

=> s l1 and l2
L3 3 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 2 DUP REM L3 (1 DUPLICATE REMOVED)

=> d 1-2 ibib ab

L4 ANSWER 1 OF 2 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 1

ACCESSION NUMBER: 2004-07314 BIOTECHDS
TITLE: New testis-specific tubulin
tyrosine-ligase-like BGS-42 polypeptide,
useful for preventing, treating or ameliorating a medical
condition, e.g. aberrant cellular proliferation, reproductive
disorders or testicular disorders;
involving vector-mediated gene transfer, expression in
host cell for use in gene therapy

AUTHOR: FEDER J N; WU S; NELSON T C
PATENT ASSIGNEE: BRISTOL-MYERS SQUIBB CO
PATENT INFO: WO 2004005487 15 Jan 2004
APPLICATION INFO: WO 2003-US21605 9 Jul 2003
PRIORITY INFO: US 2002-394725 9 Jul 2002; US 2002-394725 9 Jul 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-099381 [10]

AB DERWENT ABSTRACT:

NOVELTY - A testis-specific tubulin tyrosine-ligase-like polypeptide, designated BGS-42 polypeptide, is new.

DETAILED DESCRIPTION - A testis-specific tubulin tyrosine-ligase-like polypeptide, designated BGS-42 polypeptide comprises or consists of: (a) a polypeptide fragment, domain, epitope or the full-length protein of a fully defined sequence of 541 amino acids (I), as given in the specification, or the encoded sequence included in ATCC Deposit Number PTA-4454, having tyrosine tubulin ligase activity; (b) a polypeptide comprising amino acids 2-541 of the sequence of (I), where the amino acids 2-541 comprises a polypeptide of (I) minus the start methionine; (c) a polypeptide comprising amino acids 1-541 or 73-365 of the sequence of (I); or (d) a polypeptide comprising at least 424 contiguous amino acids of the sequence of (I). INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid molecule comprising or consisting of: (a) a polynucleotide fragment of 1838 bp (II), fully defined in the specification, or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit Number PTA-4454, which is hybridizable to the sequence of (II); (b) a polynucleotide encoding a polypeptide fragment, domain, epitope or the full-length protein of the sequence of (I), or a polypeptide fragment, domain or epitope encoded by the cDNA sequence included in ATCC Deposit Number PTA-4454, which is hybridizable to the sequence of (II), having tyrosine tubulin ligase activity; (c) a polynucleotide which is a variant or an allelic variant of (II); (d) nucleotides 156-1775 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 2-541 of (I) minus the start methionine; (e) nucleotides 153-1775 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 1-541 of (I) including the start codon; (f) nucleotides 369-1247 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 73-365 of (I); (g) a polynucleotide that encodes at least 424 contiguous amino acids of (I); (h) at least 1272 contiguous nucleotides of (II); (i) a polynucleotide which represents the complementary sequence (antisense) of (II); (j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides above, where the polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A or only T residues; (k) a polynucleotide comprising or consisting of the BGS-42 gene or BGS-42 promoter; or (l) a nucleotide sequence of 2241 bp, fully defined in the specification; (2) a recombinant vector comprising the isolated nucleic acid molecule; (3) an isolated antibody that binds specifically to BGS-42 polypeptide; (4) a recombinant host cell comprising the vector sequences, or expressing the BGS-42 polypeptide; (5) making an isolated polypeptide; (6) preventing, treating or ameliorating a medical condition; and (7) diagnosing a pathological condition or a susceptibility to a pathological condition in a subject.

WIDER DISCLOSURE - Also disclosed are screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides, and methods of controlling the expression of the polypeptide.

BIOTECHNOLOGY - Preparation (claimed): The BGS-42 polypeptide is prepared by standard recombinant methods. Making an isolated polypeptide comprises culturing the recombinant host cell under conditions such that the polypeptide is expressed, and recovering the polypeptide. Preferred

Polypeptide: The full-length protein comprises sequential amino acid deletions from the C-terminus or the N-terminus. Preferred Nucleic Acid: The polynucleotide fragment consists of a nucleotide sequence encoding a human tyrosine tubulin ligase. Preferred Method: Preventing, treating or ameliorating a medical condition comprises administering to a mammalian subject a therapeutic amount of the BGS-42 polypeptide or its modulator. Diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprises determining the presence or absence of a mutation in the polynucleotide cited above, and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of the mutation. Alternatively, the method comprises determining the presence or amount of expression of the BGS-42 polypeptide in a tyrosine tubulin ligase sample, and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

ACTIVITY - Cytostatic; Respiratory-Gen.; Gastrointestinal-Gen.; Neuroprotective; Endocrine-Gen.; Antiinflammatory; Anabolic; Hypertensive; Osteopathic; Nootropic; Antiparkinsonian; Antiarthritic; Antiasthmatic; Anti-HIV; Antibacterial; Immunosuppressive; Antiseborrheic; Dermatological. No biological data given.

MECHANISM OF ACTION - Tyrosine Ligase Modulator; Gene Therapy. No biological data given.

USE - The BGS-42 polypeptide or polynucleotide can be used for diagnosing a pathological condition or a susceptibility to a pathological condition in a subject, and for preventing, treating or ameliorating a medical condition, such as a disorder related to aberrant tubulin ligase activity, a disorder related to aberrant tubulin-carboxypeptidase activity, aberrant cellular proliferation, reproductive disorders, testicular disorders, testicular cancer, pulmonary disorders, lung cancer, gastrointestinal disorders, colon cancer, stomach cancer, neural disorders, brain cancer, liver cancer, or proliferative condition of the testis, lung, small intestine, brain or lymph tissue (all claimed). The BGS-42 polypeptide, polynucleotide, or their modulators are also useful for treating infertility, Cushing's syndrome, emphysema, pneumonia, Addison's disease, acromegaly, Alzheimer's disease, or Parkinson's disease. The BGS-42 polypeptide can be used as a preventive agent for immunological disorders including arthritis, asthma, AIDS, sepsis, acne, Sjogren's disease or scleroderma. The antibodies may be used to purify, detect and target the BGS-42 polypeptides.

ADMINISTRATION - Administration of the antibody is 0.1-100 (preferably 1-10) mg/kg, intradermally, intramuscularly, intraperitoneally, intravenously, subcutaneously, intranasally, epidurally, intraventricularly, intrathecally, topically, orally, or rectally.

EXAMPLE - A polynucleotide encoding a BGS-42 polypeptide was amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence to synthesize insertion fragments. The pQE-9 vector was digested with BamHI and XbaI and the amplified fragment was ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial ribosome-binding site. The ligation mixture was used to transform Escherichia coli strain M15/rep4. Transformants were identified by their ability to grow on LB (Luria bertani) plates, and ampicillin/kanamycin-resistant colonies were selected. Clones containing the desired constructs were grown overnight in liquid culture, i.e. LB media, supplemented with both ampicillin and kanamycin. Isopropyl-B-D-thiogalacto pyranoside (IPTG) was added to induce gene expression. Cells were grown for an extra 3-4 hours, and cells were harvested by centrifugation. The cell pellet obtained by centrifugation was solubilized, and the solubilized BGS-42 protein was purified using a metal chelating column under conditions that allow tight binding of the protein. (343 pages)

DOCUMENT NUMBER: 141:238811
TITLE: Protein and cDNA sequences of a novel human testis-specific tubulin tyrosine ligase like protein BGS-42, and diagnostic and therapeutic use
INVENTOR(S): Feder, John N.; Nelson, Thomas C.; Wu, Shujian; Krystek, Stanley R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 199 pp., Cont.-in-part of U.S. Ser. No. 615,659.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004171131 | A1 | 20040902 | US 2003-635977 | 20030807 |
| US 2004157234 | A1 | 20040812 | US 2003-615659 | 20030709 |
| PRIORITY APPLN. INFO.: | | | US 2002-394725P | P 20020709 |
| | | | US 2003-615659 | A2 20030709 |

AB The present invention provides novel polynucleotides encoding BGS-42 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel BGS-42 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

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FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCPLUS, NTIS, LIFESCI' ENTERED AT 12:09:07 ON 28 FEB 2006

L1 7010 S TESTIS (W) SPECIFIC
L2 431 S TYROSINE (W)LIGASE?
L3 3 S L1 AND L2
L4 2 DUP REM L3 (1 DUPLICATE REMOVED)

=> s tubulin (a) 12
L5 405 TUBULIN (A) L2

=> s clon? or express? or recombinant
L6 7556238 CLON? OR EXPRESS? OR RECOMBINANT

=> s 15 and 16
L7 83 L5 AND L6

=> dup rem 17
PROCESSING COMPLETED FOR L7
L8 39 DUP REM L7 (44 DUPLICATES REMOVED)

=> d 1-39 ibib ab

L8 ANSWER 1 OF 39 HCPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2005:156228 HCPLUS
Correction of: 2005:16967
DOCUMENT NUMBER: 142:192331
Correction of: 142:108390

TITLE: Quantitative RT-PCR method for the detection in blood
 of microarray-identified rheumatoid arthritis-related
 gene transcripts for diagnosing and monitoring disease
 state
 INVENTOR(S): Liew, Choong-Chin
 PATENT ASSIGNEE(S): ChondroGene Limited, Can.
 SOURCE: U.S. Pat. Appl. Publ., 81 pp., Cont.-in-part of U.S.
 Ser. No. 802,875.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 47
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2005003394 | A1 | 20050106 | US 2004-812782 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| US 2005003394 | A1 | 20050106 | US 2004-812782 | 20040330 |
| US 2005003394 | A1 | 20050106 | US 2004-812782 | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812782 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood for diagnosing and monitoring diseases. The present invention demonstrates that a simple drop of blood may be used to determine the quant. expression of various mRNAs that reflect the health/disease state of the subject through the use of quant. reverse transcription-polymerase chain reaction (QRT-PCR) anal. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring rheumatoid arthritis using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

L8 ANSWER 2 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1311496 HCAPLUS
 DOCUMENT NUMBER: 144:49649
 TITLE: Association of gene expression profiles with
 asthma in peripheral blood cells
 INVENTOR(S): Kachalsky, Sylvia G.; Horev, Guy
 PATENT ASSIGNEE(S): Linkagene Ltd., Israel
 SOURCE: PCT Int. Appl., 74 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2005118403 | A2 | 20051215 | WO 2005-IL590 | 20050605 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, | | | | |

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
 NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
 ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-576599P P 20040604

AB The present invention relates to methods of identifying biomarkers for disease, which comprise measuring gene expression levels in subpopulations of blood cells obtained from subjects of closed populations. Particularly, the present invention relates to methods of diagnosing, monitoring and prognosing diseases comprising determining expression levels of disease-specific genes. Thus, a library of about 41,500 cDNA clones derived from the I.M.A.G.E consortium was printed in microarrays comprising the whole transcriptome and used to screen RNA isolated from leukocytes from a Cochin Jewish population known as susceptible to high occurrences of asthma. Comparison of expression profiles from asthma and non-asthma individuals identified 783 biomarker transcripts for asthma.

L8 ANSWER 3 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:984082 HCAPLUS

DOCUMENT NUMBER: 143:280551

TITLE: Human glucocorticoid receptor coactivator STAMP modulating glucocorticoid-responsive gene expression, its orangutan and green monkey homolog, and therapeutic use thereof

INVENTOR(S): Simons, S. Stoney, Jr.; He, Yuanzheng

PATENT ASSIGNEE(S): Government of the United States of America as Represented by the Secretary of the Department of Health and Human Services, USA

SOURCE: PCT Int. Appl., 235 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2005082935 | A1 | 20050909 | WO 2005-US6393 | 20050225 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: US 2004-548039P P 20040226

AB The invention provides a new glucocorticoid receptor (GR) coactivator named STAMP (SRC-1 and TIF2 Associated Modulatory Protein) that can modulate transcription of glucocorticoid-responsive genes. The isolated STAMP gene is located on chromosome 14q24.3 and contains 32 introns, and its encodes a 1277 amino acid protein (predominant form, with predicted mol. weight of 143 kDa) or a 1281 amino acid protein with four extra amino acid at

N-terminus. Activity of STAMP in GR-mediated induction. STAMP and TIF2 act cooperatively to modulate glucocorticoid receptor activity and STAMP activity requires the RID (receptor interaction domain) domains (around residues 834-1277) that mediate TIF2 binding to GR and/or STAMP. Also provided are siRNAs shown to inhibit STAMP actions. The invention also provides antibodies that can bind STAMP and modulate its activity. In addition, the invention provides antisense, ribozyme and siRNA STAMP nucleic acids that can modulate the expression of STAMP. Also provided are compns. and methods for modulating glucocorticoid-responsive gene expression and for treating a variety of diseases and conditions.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:497356 HCAPLUS
 DOCUMENT NUMBER: 143:39118
 TITLE: Gene expression profiling for diagnosis, prognosis, and therapy of osteoarthritis and other diseases using microarrays
 INVENTOR(S): Liew, Choong-chin
 PATENT ASSIGNEE(S): ChondroGene Limited, Can.
 SOURCE: U.S. Pat. Appl. Publ., 157 pp., Cont.-in-part of U.S. Ser. No. 802,875.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 47
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2005123938 | A1 | 20050609 | US 2004-809675 | 20040325 |
| US 2004037841 | A1 | 20040226 | US 2002-85783 | 20020228 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2005123938 | A1 | 20050609 | US 2004-809675 | 20040325 |
| US 2005123938 | A1 | 20050609 | US 2004-809675 | 20040325 |
| US 2004248169 | A1 | 20041209 | US 2004-812737 | 20040330 |
| WO 2004112589 | A2 | 20041229 | WO 2004-US20836 | 20040621 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

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|------------------------|-----------------|-------------|
| PRIORITY APPLN. INFO.: | US 1999-115125P | P 19990106 |
| | US 2000-477148 | B1 20000104 |
| | US 2001-271955P | P 20010228 |
| | US 2001-275017P | P 20010312 |
| | US 2001-305340P | P 20010713 |
| | US 2002-85783 | A2 20020228 |
| | US 2002-268730 | A2 20021009 |
| | US 2003-601518 | A2 20030620 |
| | US 2004-802875 | A2 20040312 |
| | US 2004-809675 | A 20040325 |

AB The present invention relates to gene expression profiling for diagnosis, prognosis and therapy of osteoarthritis and other diseases using microarray methods. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.]

L8 ANSWER 5 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:325595 HCAPLUS

DOCUMENT NUMBER: 142:353388

TITLE: Gene expression profiles and biomarkers for the detection of Alzheimer's disease-related and other disease-related gene transcripts in blood

INVENTOR(S): Liew, Choong-chin

PATENT ASSIGNEE(S): Chondrogene Ltd., Can.

SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S. Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 47

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2005079514 | A1 | 20050414 | US 2004-812827 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular Alzheimer's disease, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess

the effect of a particular treatment regimen.

L8 ANSWER 6 OF 39 HCPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:160724 HCPLUS
DOCUMENT NUMBER: 142:259424
TITLE: Gene expression profiles and biomarkers for the detection of asthma-related and other disease-related gene transcripts in blood
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): ChondroGene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 47
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2005042630 | A1 | 20050224 | US 2004-816357 | 20040401 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| US 2005042630 | A1 | 20050224 | US 2004-816357 | 20040401 |
| US 2005042630 | A1 | 20050224 | US 2004-816357 | 20040401 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-816357 | A 20040401 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular asthma, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of three records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 7 OF 39 HCPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:499078 HCPLUS
DOCUMENT NUMBER: 143:23514
TITLE: A vital role of tubulin-tyrosine-ligase for neuronal organization
AUTHOR(S): Erck, Christian; Peris, Leticia; Andrieux, Annie; Meissirel, Claire; Gruber, Achim D.; Vernet, Muriel; Schweitzer, Annie; Saoudi, Yasmine; Pointu, Herve; Bosc, Christophe; Salin, Paul A.; Job, Didier;

CORPORATE SOURCE: Wehland, Juergen
Department of Cell Biology, German Research Center for Biotechnology, Braunschweig, D-38124, Germany
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2005), 102(22), 7853-7858
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tubulin is subject to a special cycle of detyrosination/tyrosination in which the C-terminal tyrosine of α -tubulin is cyclically removed by a carboxypeptidase and readded by a tubulin-tyrosine-ligase (TTL). This tyrosination cycle is conserved in evolution, yet its physiol. importance is unknown. Here, we find that TTL suppression in mice causes perinatal death. A minor pool of tyrosinated (Tyr-)tubulin persists in TTL null tissues, being present mainly in dividing TTL null cells where it originates from tubulin synthesis, but it is lacking in postmitotic TTL null cells such as neurons, which is apparently deleterious because early death in TTL null mice is, at least in part, accounted for by a disorganization of neuronal networks, including a disruption of the cortico-thalamic loop. Correlatively, cultured TTL null neurons display morphogenetic anomalies including an accelerated and erratic time course of neurite outgrowth and a premature axonal differentiation. These anomalies may involve a mislocalization of CLIP170, which we find lacking in neurite extensions and growth cones of TTL null neurons. Our results demonstrate a vital role of TTL for neuronal organization and suggest a requirement of Tyr-tubulin for proper control of neurite extensions.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 39 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:276126 SCISEARCH
THE GENUINE ARTICLE: 902DT
TITLE: Global effects of BCR/ABL and TEL/PDGFR beta expression on the proteome and phosphoproteome - Identification of the rho pathway as a target of BCR/ABL
AUTHOR: Unwin R D; Sternberg D W; Lu Y N; Pierce A; Gilliland D G; Whetton A D (Reprint)
COPORATE SOURCE: Univ Manchester, Christie Hosp, Fac Med & Human Sci, Manchester M20 9BX, Lancs, England (Reprint); Univ Manchester, Fac Med & Human Sci, Manchester M20 9BX, Lancs, England; Christie Hosp, Paterson Inst Canc Res, Inst Mass Spectrometry, Manchester M20 9BX, Lancs, England; Harvard Univ, Sch Med, Brigham & Womens Hosp, Div Hematol, Boston, MA 02115 USA; Mt Sinai Sch Med, New York, NY 10029 USA; Howard Hughes Med Inst, Chevy Chase, MD 20815 USA
awhetton@picr.man.ac.uk
COUNTRY OF AUTHOR: England; USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (25 FEB 2005) Vol. 280, No. 8, pp. 6316-6326.
ISSN: 0021-9258.
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 80
ENTRY DATE: Entered STN: 18 Mar 2005
Last Updated on STN: 18 Mar 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Many leukemic oncogenes form as a consequence of gene fusions or mutation that result in the activation or overexpression of a tyrosine

kinase. To identify commonalities and differences in the action of two such kinases, breakpoint cluster region (BCR)/ABL and TEL/PDGFRbeta, two-dimensional gel electrophoresis was employed to characterize their effects on the proteome. While both oncogenes affected expression of specific proteins, few common effects were observed. A number of proteins whose expression is altered by BCR/ABL, including gelsolin and stathmin, are related to cytoskeletal function whereas no such changes were seen in TEL/PDGFRbeta-transfected cells. Treatment of cells with the kinase inhibitor ST1571 for 4-h reversed changes in expression of some of these cytoskeletal proteins. Correspondingly, BCR/ABL-transfected cells were less responsive to chemotactic and chemokinetic stimuli than non-transfected cells and TEI/PDGFRbeta-transfected Ba/F3 cells. Decreased motile response was reversed by a 16-h treatment with ST1571. A phosphoprotein-specific gel stain was used to identify TEL/PDGFRbeta and BCR/ABL-mediated changes in the phosphoproteome. These included changes on Crkl, Ras-GAP-binding protein 1, and for BCR/ABL, cytoskeletal proteins such as tubulin, and Nedd5. Decreased phosphorylation of Rho-GTPase dissociation inhibitor (Rho GDI) was also observed in BCR/ABL-transfected cells. This results in the activation of the Rho pathway, and treatment of cells with Y27632, an inhibitor of Rho kinase, inhibited DNA synthesis in BCR/ABL-transfected Ba/F3 cells but not TEL/PDGFRB-expressing cells. Expression of a dominant-negative RhoA inhibited both DNA synthesis and transwell migration, demonstrating the significance of this pathway in BCR/ABL-mediated transformation.

L8 ANSWER 9 OF 39 MEDLINE on STN
ACCESSION NUMBER: 2005313865 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15890843
TITLE: Tubulin polyglutamylase enzymes are members of the TTL domain protein family.
AUTHOR: Janke Carsten; Rogowski Krzysztof; Wloga Dorota; Regnard Catherine; Kajava Andrey V; Strub Jean-Marc; Temurak Nevzat; van Dijk Juliette; Boucher Dominique; van Dorsselaer Alain; Suryavanshi Swati; Gaertig Jacek; Edde Bernard
CORPORATE SOURCE: Centre de Recherches de Biochimie Macromoleculaire, CNRS, 34293 Montpellier, France.
SOURCE: Science, (2005 Jun 17) Vol. 308, No. 5729, pp. 1758-62.
Electronic Publication: 2005-05-12..
Journal code: 0404511. E-ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 20050618
Last Updated on STN: 20050701
Entered Medline: 20050630
AB Polyglutamylation of tubulin has been implicated in several functions of microtubules, but the identification of the responsible enzyme(s) has been challenging. We found that the neuronal tubulin polyglutamylase is a protein complex containing a tubulin tyrosine ligase-like (TTL) protein, TTLL1. TTLL1 is a member of a large family of proteins with a TTL homology domain, whose members could catalyze ligations of diverse amino acids to tubulins or other substrates. In the model protist *Tetrahymena thermophila*, two conserved types of polyglutamylases were characterized that differ in substrate preference and subcellular localization.

L8 ANSWER 10 OF 39 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:412589 SCISEARCH
THE GENUINE ARTICLE: 914YX

TITLE: 3-Nitrotyrosine attenuates respiratory syncytial virus infection in human bronchial epithelial cell line

AUTHOR: Huang Y C T (Reprint); Li Z W; Brighton L E; Carson J L; Becker S; Soukup J M

CORPORATE SOURCE: CB 7315, 104 Mason Farm Rd, Chapel Hill, NC 27599 USA (Reprint); US EPA, Natl Hlth & Environm Effects Res Lab, Off Res & Dev, Res Triangle Pk, NC 27711 USA; Univ N Carolina, Ctr Environm Med Asthma & Lung Biol, Chapel Hill, NC USA
huang.tony@epa.gov

COUNTRY OF AUTHOR: USA

SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY, (MAY 2005) Vol. 288, No. 5, pp. L988-L996.

ISSN: 1040-0605.

PUBLISHER: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 55

ENTRY DATE: Entered STN: 28 Apr 2005
Last Updated on STN: 28 Apr 2005

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB 3-Nitrotyrosine (NO₂Tyr), an L-tyrosine derivative during nitratative stress, can substitute the COOH-terminal tyrosine of alpha-tubulin, posttranslationally altering microtubular functions. Because infection of the cells by respiratory syncytial virus (RSV) may require intact microtubules, we tested the hypothesis that NO₂Tyr would inhibit RSV infection and intracellular signaling via nitrotyrosination of alpha-tubulin. A human bronchial epithelial cell line (BEAS-2B) was incubated with RSV with or without NO₂Tyr. The release of chemokines and viral particles and activation of interferon regulatory factor-3 (IRF-3) were measured. Incubation with NO₂Tyr increased nitrotyrosinated alpha-tubulin, and NO₂Tyr colocalized with microtubules. RSV-infected cells released viral particles, RANTES, and IL-8 in a time- and dose-dependent manner, and intracellular RSV proteins coprecipitated with alpha-tubulin. NO₂Tyr attenuated the RSV- induced release of RANTES, IL-8, and viral particles by 50-90% and decreased alpha-tubulin-associated RSV proteins. 3-Chlorotyrosine, another L-tyrosine derivative, had no effects. NO₂Tyr also inhibited the RSV- induced shift of the unphosphorylated form I of IRF-3 to the phosphorylated form II. Pre-exposure of the cells to NO₂ (0.15 ppm, 4 h), which produced diffuse protein tyrosine nitration, did not affect RSV- induced release of RANTES, IL-8, or viral particles. NO₂Tyr did not affect the potential of viral spreading to the neighboring cells since the RSV titers were not decreased when the uninfected cells were cocultured with the preinfected cells in NO₂Tyr-containing medium. These results indicate that NO₂Tyr, by replacing the COOH-terminal tyrosine of alpha-tubulin, attenuated RSV infection, and the inhibition appeared to occur at the early stages of RSV infection.

L8 ANSWER 11 OF 39 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 2

ACCESSION NUMBER: 2004-07314 BIOTECHDS

TITLE: New testis-specific tubulin tyrosine-ligase-like BGS-42 polypeptide, useful for preventing, treating or ameliorating a medical condition, e.g. aberrant cellular proliferation, reproductive disorders or testicular disorders; involving vector-mediated gene transfer, expression in host cell for use in gene therapy

AUTHOR: FEDER J N; WU S; NELSON T C

PATENT ASSIGNEE: BRISTOL-MYERS SQUIBB CO

PATENT INFO: WO 2004005487 15 Jan 2004

APPLICATION INFO: WO 2003-US21605 9 Jul 2003

PRIORITY INFO: US 2002-394725 9 Jul 2002; US 2002-394725 9 Jul 2002

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2004-099381 [10]

AB DERWENT ABSTRACT:

NOVELTY - A testis-specific tubulin tyrosine-ligase-like polypeptide, designated BGS-42 polypeptide, is new.

DETAILED DESCRIPTION - A testis-specific tubulin tyrosine-ligase-like polypeptide, designated BGS-42

polypeptide comprises or consists of: (a) a polypeptide fragment, domain, epitope or the full-length protein of a fully defined sequence of 541 amino acids (I), as given in the specification, or the encoded sequence included in ATCC Deposit Number PTA-4454, having tyrosine tubulin ligase activity; (b) a polypeptide comprising amino acids 2-541 of the sequence of (I), where the amino acids 2-541 comprises a polypeptide of (I) minus the start methionine; (c) a polypeptide comprising amino acids 1-541 or 73-365 of the sequence of (I); or (d) a polypeptide comprising at least 424 contiguous amino acids of the sequence of (I). INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid molecule comprising or consisting of: (a) a polynucleotide fragment of 1838 bp (II), fully defined in the specification, or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit Number PTA-4454, which is hybridizable to the sequence of (II); (b) a polynucleotide encoding a polypeptide fragment, domain, epitope or the full-length protein of the sequence of (I), or a polypeptide fragment, domain or epitope encoded by the cDNA sequence included in ATCC Deposit Number PTA-4454, which is hybridizable to the sequence of (II), having tyrosine tubulin ligase activity; (c) a polynucleotide which is a variant or an allelic variant of (II); (d) nucleotides 156-1775 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 2-541 of (I) minus the start methionine; (e) nucleotides 153-1775 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 1-541 of (I) including the start codon; (f) nucleotides 369-1247 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 73-365 of (I); (g) a polynucleotide that encodes at least 424 contiguous amino acids of (I); (h) at least 1272 contiguous nucleotides of (II); (i) a polynucleotide which represents the complementary sequence (antisense) of (II); (j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides above, where the polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A or only T residues; (k) a polynucleotide comprising or consisting of the BGS-42 gene or BGS-42 promoter; or (l) a nucleotide sequence of 2241 bp, fully defined in the specification; (2) a recombinant vector comprising the isolated nucleic acid molecule; (3) an isolated antibody that binds specifically to BGS-42 polypeptide; (4) a recombinant host cell comprising the vector sequences, or expressing the BGS-42 polypeptide; (5) making an isolated polypeptide; (6) preventing, treating or ameliorating a medical condition; and (7) diagnosing a pathological condition or a susceptibility to a pathological condition in a subject.

WIDER DISCLOSURE - Also disclosed are screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides, and methods of controlling the expression of the polypeptide.

BIOTECHNOLOGY - Preparation (claimed): The BGS-42 polypeptide is prepared by standard recombinant methods. Making an isolated polypeptide comprises culturing the recombinant host cell under conditions such that the polypeptide is expressed, and recovering the polypeptide. Preferred Polypeptide: The full-length protein comprises sequential amino acid deletions from the C-terminus or the N-terminus. Preferred Nucleic Acid: The polynucleotide fragment consists of a nucleotide sequence encoding a human tyrosine tubulin ligase. Preferred Method: Preventing, treating or ameliorating a medical

condition comprises administering to a mammalian subject a therapeutic amount of the BGS-42 polypeptide or its modulator. Diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprises determining the presence or absence of a mutation in the polynucleotide cited above, and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of the mutation. Alternatively, the method comprises determining the presence or amount of expression of the BGS-42 polypeptide in a tyrosine tubulin ligase sample, and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

ACTIVITY - Cytostatic; Respiratory-Gen.; Gastrointestinal-Gen.; Neuroprotective; Endocrine-Gen.; Antiinflammatory; Anabolic; Hypertensive; Osteopathic; Nootropic; Antiparkinsonian; Antiarthritic; Antiasthmatic; Anti-HIV; Antibacterial; Immunosuppressive; Antiseborrheic; Dermatological. No biological data given.

MECHANISM OF ACTION - Tyrosine Ligase Modulator; Gene Therapy. No biological data given.

USE - The BGS-42 polypeptide or polynucleotide can be used for diagnosing a pathological condition or a susceptibility to a pathological condition in a subject, and for preventing, treating or ameliorating a medical condition, such as a disorder related to aberrant tubulin ligase activity, a disorder related to aberrant tubulin-carboxypeptidase activity, aberrant cellular proliferation, reproductive disorders, testicular disorders, testicular cancer, pulmonary disorders, lung cancer, gastrointestinal disorders, colon cancer, stomach cancer, neural disorders, brain cancer, liver cancer, or proliferative condition of the testis, lung, small intestine, brain or lymph tissue (all claimed). The BGS-42 polypeptide, polynucleotide, or their modulators are also useful for treating infertility, Cushing's syndrome, emphysema, pneumonia, Addison's disease, acromegaly, Alzheimer's disease, or Parkinson's disease. The BGS-42 polypeptide can be used as a preventive agent for immunological disorders including arthritis, asthma, AIDS, sepsis, acne, Sjogren's disease or scleroderma. The antibodies may be used to purify, detect and target the BGS-42 polypeptides.

ADMINISTRATION - Administration of the antibody is 0.1-100 (preferably 1-10) mg/kg, intradermally, intramuscularly, intraperitoneally, intravenously, subcutaneously, intranasally, epidurally, intraventricularly, intrathecally, topically, orally, or rectally.

EXAMPLE - A polynucleotide encoding a BGS-42 polypeptide was amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence to synthesize insertion fragments. The pQE-9 vector was digested with BamHI and XbaI and the amplified fragment was ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial ribosome-binding site. The ligation mixture was used to transform Escherichia coli strain M15/rep4. Transformants were identified by their ability to grow on LB (Luria bertani) plates, and ampicillin/kanamycin-resistant colonies were selected. Clones containing the desired constructs were grown overnight in liquid culture, i.e. LB media, supplemented with both ampicillin and kanamycin. Isopropyl-B-D-thiogalacto pyranoside (IPTG) was added to induce gene expression. Cells were grown for an extra 3-4 hours, and cells were harvested by centrifugation. The cell pellet obtained by centrifugation was solubilized, and the solubilized BGS-42 protein was purified using a metal chelating column under conditions that allow tight binding of the protein. (343 pages)

L8 ANSWER 12 OF 39 HCPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2005:156681 HCPLUS
Correction of: 2005:60757

DOCUMENT NUMBER: 142:216629
Correction of: 142:132329

TITLE: Gene expression profiles and biomarkers for

INVENTOR(S) : the detection of hyperlipidemia and other
 disease-related gene transcripts in blood
 Liew, Choong-Chin
 PATENT ASSIGNEE(S) : Chondrogene Limited, Can.
 SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S.
 Ser. No. 802,875.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 47
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004248170 | A1 | 20041209 | US 2004-812777 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004248170 | A1 | 20041209 | US 2004-812777 | 20040330 |
| US 2004248170 | A1 | 20041209 | US 2004-812777 | 20040330 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812777 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular hyperlipidemia, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

L8 ANSWER 13 OF 39 HCPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:824055 HCPLUS
 DOCUMENT NUMBER: 141:330185
 TITLE: Gene expression profiling for diagnosis and treatment of angiogenesis-related disorders
 INVENTOR(S) : Gonda, Thomas John; Kremmidiotis, Gabriel
 PATENT ASSIGNEE(S) : Bionomics Limited, Australia
 SOURCE: PCT Int. Appl., 148 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2004085675 | A1 | 20041007 | WO 2004-AU383 | 20040326 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, | | | | |

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
 SK, TR, BF, BJ, CF, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
 TD, TG

EP 1608778 A1 20051228 EP 2004-723453 20040326

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

PRIORITY APPLN. INFO.: AU 2003-901511 A 20030328
 WO 2004-AU383 W 20040326

AB The present invention provides methods of gene expression profiling for diagnosis and treatment of angiogenesis-related disorders. Diseases of the invention include cancer, rheumatoid arthritis, diabetic retinopathy, psoriasis, cardiovascular diseases such as atherosclerosis, ischmeic limb disease and coronary heart disease.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 39 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1997 HCPLUS

DOCUMENT NUMBER: 142:111841

TITLE: Gene expression profiles and biomarkers for the detection of depression-related and other disease-related gene transcripts in blood

INVENTOR(S): Liew, Choong-Chin

PATENT ASSIGNEE(S): Chondrogenic Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 47

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004265868 | A1 | 20041230 | US 2004-812702 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| US 2004265868 | A1 | 20041230 | US 2004-812702 | 20040330 |
| US 2004265868 | A1 | 20041230 | US 2004-812702 | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812702 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular mental depression, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy,

systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

L8 ANSWER 15 OF 39 HCPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:60760 HCPLUS
 Correction of: 2004:1036573
 DOCUMENT NUMBER: 142:153477
 Correction of: 142:16776
 TITLE: Gene expression profiles and biomarkers for the detection of Chagas disease and other disease-related gene transcripts in blood
 INVENTOR(S): Liew, Choong-Chin
 PATENT ASSIGNEE(S): Chondrogenic Limited, Can.
 SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 802,875.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 47
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004241729 | A1 | 20041202 | US 2004-813097 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004241729 | A1 | 20041202 | US 2004-813097 | 20040330 |
| US 2004241729 | A1 | 20041202 | US 2004-813097 | 20040330 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-813097 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular Chagas disease, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.]

L8 ANSWER 16 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:60759 HCAPLUS
 Correction of: 2004:1036572
 DOCUMENT NUMBER: 142:111840
 Correction of: 142:16824
 TITLE: Gene expression profiles and biomarkers for
 the detection of lung disease-related and other
 disease-related gene transcripts in blood
 INVENTOR(S): Liew, Choong-Chin
 PATENT ASSIGNEE(S): Chondrogene Limited, Can.
 SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S.
 Ser. No. 802,875.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 47
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004241728 | A1 | 20041202 | US 2004-812764 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004241728 | A1 | 20041202 | US 2004-812764 | 20040330 |
| US 2004241728 | A1 | 20041202 | US 2004-812764 | 20040330 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812764 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

L8 ANSWER 17 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:60754 HCAPLUS
 Correction of: 2004:1036571
 DOCUMENT NUMBER: 142:233342
 Correction of: 142:16836
 TITLE: Sequences of human schizophrenia related genes and use
 for diagnosis, prognosis and therapy
 INVENTOR(S): Liew, Choong-Chin
 PATENT ASSIGNEE(S): Chondrogene Limited, Can.
 SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S.
 Ser. No. 802,875.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 47

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004241727 | A1 | 20041202 | US 2004-812731 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004241727 | A1 | 20041202 | US 2004-812731 | 20040330 |
| US 2004241727 | A1 | 20041202 | US 2004-812731 | 20040330 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| US 2005208519 | A1 | 20050922 | US 2004-989191 | 20041115 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812731 | A 20040330 |
| | | | WO 2004-US20836 | A2 20040621 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 18 OF 39 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:60755 HCPLUS

Correction of: 2004:1036570

DOCUMENT NUMBER: 142:154259

Correction of: 142:36938

TITLE: Analysis of genetic information contained in peripheral blood for diagnosis, prognosis and monitoring treatment of allergy, infection and genetic disease in human

INVENTOR(S): Liew, Choong-Chin

PATENT ASSIGNEE(S): Chondrogenic Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S. Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 47

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2004241726 | A1 | 20041202 | US 2004-812707 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |

| | | | | |
|------------------------|----|----------|-----------------|-------------|
| US 2004241726 | A1 | 20041202 | US 2004-812707 | 20040330 |
| US 2004241726 | A1 | 20041202 | US 2004-812707 | 20040330 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812707 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular allergy, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 19 OF 39 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:722839 HCPLUS

DOCUMENT NUMBER: 141:238811

TITLE: Protein and cDNA sequences of a novel human testis-specific tubulin tyrosine ligase like protein BGS-42, and diagnostic and therapeutic use

INVENTOR(S): Feder, John N.; Nelson, Thomas C.; Wu, Shujian; Krystek, Stanley R.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 199 pp., Cont.-in-part of U.S. Ser. No. 615,659.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004171131 | A1 | 20040902 | US 2003-635977 | 20030807 |
| US 2004157234 | A1 | 20040812 | US 2003-615659 | 20030709 |
| PRIORITY APPLN. INFO.: | | | US 2002-394725P | P 20020709 |
| | | | US 2003-615659 | A2 20030709 |

AB The present invention provides novel polynucleotides encoding BGS-42 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel BGS-42 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

L8 ANSWER 20 OF 39

MEDLINE on STN

DUPLICATE 4

ACCESSION NUMBER: 2004470309 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15382060
TITLE: Low expression of human tubulin tyrosine ligase and suppressed tubulin tyrosination/detyrosination cycle are associated with impaired neuronal differentiation in neuroblastomas with poor prognosis.
AUTHOR: Kato Chiaki; Miyazaki Kou; Nakagawa Atsuko; Ohira Miki; Nakamura Yohko; Ozaki Toshinori; Imai Toshio; Nakagawara Akira
CORPORATE SOURCE: Division of Biochemistry, Chiba Cancer Center Research Institute, Chiba, Japan.
SOURCE: International journal of cancer. Journal international du cancer, (2004 Nov 10) Vol. 112, No. 3, pp. 365-75.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20040922
Last Updated on STN: 20041219
Entered Medline: 20041202
AB Neuroblastoma (NBL), one of the most common childhood solid tumors, has a distinct nature in different prognostic subgroups. However, the precise mechanism underlying this phenomenon remains largely unknown. To understand the molecular and genetic bases of neuroblastoma, we have generated its cDNA libraries and identified a human ortholog of tubulin tyrosine ligase gene (hTTL/Nbla0660) as a differentially expressed gene at high levels in a favorable subset of the tumor. Tubulin is subjected to several types of evolutionarily conserved posttranslational modification, including tyrosination and detyrosination. Tubulin tyrosine ligase catalyzes ligation of the tyrosine residue to the COOH terminus of the detyrosinated form of alpha-tubulin. The measurement of hTTL mRNA expression in 74 primary neuroblastomas by quantitative real-time reverse transcription-PCR revealed that its high expression was significantly associated with favorable stages (1, 2 and 4s; p = 0.0069), high TrkA expression (p = 0.002), a single copy of MYCN (p < 0.00005), tumors found by mass screening (p = 0.0042), nonadrenal origin (p = 0.0042) and good prognosis (p = 0.023). The log-rank test showed that high expression of hTTL was an indicator of favorable prognosis (p = 0.026). Immunohistochemical analysis using specific antibodies generated by us demonstrated that tyrosinated tubulin (Tyr-tubulin), detyrosinated tubulin (Glu-tubulin) and hTTL as well as Delta2-tubulin were positive in favorable tumors, whereas only Delta2-tubulin was positive in the tumors with MYCN amplification. In an RTBM1 neuroblastoma cell line, hTTL was increased after treating the cells with bone morphogenetic protein 2 (BMP2) or all-trans retinoic acid (RA), which induced neuronal differentiation. These results suggest that the deregulated tubulin tyrosination/detyrosination cycle caused by decreased expression of hTTL is associated with inhibition of neuronal differentiation and enhancement of cell growth in the primary neuroblastomas with poor outcome.

L8 ANSWER 21 OF 39 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004018647 EMBASE
TITLE: Endophyte-Infected Tall Fescue Diet Alters Gene Expression in Heifer Luteal Tissue as Revealed by Interspecies Microarray Analysis.
AUTHOR: Jones K.L.; King S.S.; Iqbal M.J.
CORPORATE SOURCE: K.L. Jones, Dept. of Anim. Sci., Food and Nutr., S. Illinois University Carbondale, MC 4417, 1205 Lincoln

SOURCE: Drive, Carbondale, IL 62901, United States. kljones@siu.edu
Molecular Reproduction and Development, (2004) Vol. 67, No.
2, pp. 154-161. .
Refs: 66
ISSN: 1040-452X CODEN: MREDEE

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
021 Developmental Biology and Teratology
052 Toxicology

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040129
Last Updated on STN: 20040129

AB Cattle consuming endophyte-infected tall fescue grass have an associated reduction in circulating progesterone and reduced reproductive rates. In this study, commercially available rat microarrays were used to analyze the gene expression in luteal tissues from heifers fed endophyte-free fescue, endophyte-infected fescue, or endophyte-infected fescue supplemented with the dopamine (DA) antagonist, domperidone. The number of hybridized spots represented approximately 40% of the total 10,000 rat genes/ESTs evaluated. Each luteal sample was analyzed in triplicate, resulting in within treatment correlation coefficients of ≥ 0.98 . Median values of mRNA abundance from luteal tissue taken from the endophyte-infected fed heifers revealed 598 genes and ESTs that were down regulated and 56 genes and ESTs that were upregulated compared with luteal mRNA values from the endophyte-free treatment. There were fewer comparative differences between median values from luteal mRNA from the endophyte-free versus feeding endophyte-infected plus domperidone treated heifers. Only 19 genes and ESTs were upregulated and two were down-regulated. .COPYRGT. 2004 Wiley-Liss, Inc.

L8 ANSWER 22 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:737915 HCAPLUS
DOCUMENT NUMBER: 139:256359
TITLE: Human cDNA sequences and their encoded proteins and diagnostic and therapeutic uses
INVENTOR(S): Zerhusen, Bryan D.; Paturajan, Meera; Kekuda, Ramesh; Miller, Charles E.; Rieger, Daniel K.; Pena, Carol E. A.; Shimkets, Richard A.; Li, Li; Berghs, Constance; Zhong, Mei; Casman, Stacie J.; Voss, Edward Z.; Boldog, Ferenc L.; Padigaru, Muralidhara; Smithson, Glennda; Shenoy, Suresh G.; Ji, Weizhen; Gorman, Linda; Vernet, Corine A. M.; Leite, Mario W.; Guo, Xiaoja; Anderson, David W.; Spytek, Kimberly A.; Gerlach, Valerie L.; Burgess, Catherine E.; Khramtsov, Nikolai V.; Ort, Tatiana; Ellerman, Karen; Rastelli, Luca; Agee, Michele L.; Chaudhuri, Amitabha; Chant, John S.; Dipippo, Vincent A.; Edinger, Shlomit; Eisen, Andrew; Gangolli, Esha A.; Giot, Loic; Ooi, Chean Eng; Rothenberg, Mark E.; Spaderna, Steven K.; Hjalt, Tord; Liu, Xiaohong; Taupier, Raymond J., Jr.; Catterton, Elina
PATENT ASSIGNEE(S): Curagen Corporation, USA
SOURCE: PCT Int. Appl., 562 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 159
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| WO 2003076642 | A2 | 20030918 | WO 2002-US24459 | 20020802 |

WO 2003076642 A3 20041014
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
 CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 US 2004014053 A1 20040122 US 2002-210130 20020801
 CA 2449341 AA 20030918 CA 2002-2449341 20020802
 EP 1492807 A2 20050105 EP 2002-806720 20020802
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI, CY, TR, BG, CZ, EE, SK
 JP 2005526507 T2 20050908 JP 2003-574839 20020802
 PRIORITY APPLN. INFO.: US 2001-309501P P 20010802
 US 2001-310291P P 20010803
 US 2001-310951P P 20010808
 US 2001-311292P P 20010809
 US 2001-311979P P 20010813
 US 2001-312203P P 20010814
 US 2001-313156P P 20010817
 US 2001-313201P P 20010817
 US 2001-313702P P 20010820
 US 2001-314031P P 20010821
 US 2001-314466P P 20010823
 US 2001-315403P P 20010828
 US 2001-315853P P 20010829
 US 2001-316508P P 20010831
 US 2001-323936P P 20010921
 US 2001-338078P P 20011203
 US 2002-354655P P 20020205
 US 2002-361764P P 20020305
 US 2002-373825P P 20020419
 US 2002-380971P P 20020515
 US 2002-380980P P 20020515
 US 2002-381039P P 20020516
 US 2002-383761P P 20020528
 US 2002-383887P P 20020529
 US 2002-210130 A2 20020801
 US 2001-313643P P 20010820
 US 2001-322716P P 20010917
 WO 2002-US24459 W 20020802

AB Disclosed herein are 49 cDNA sequences that encode novel human polypeptides that are members of various protein families. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivs., variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

L8 ANSWER 23 OF 39 MEDLINE on STN DUPLICATE 5
 ACCESSION NUMBER: 2003493733 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14571137
 TITLE: Cloning and genomic organization of the TTL gene on mouse chromosome 2 and human chromosome 2q13.
 AUTHOR: Erck C; MacLeod R A F; Wehland J
 CORPORATE SOURCE: Department of Cell Biology, German Research Center of Biotechnology, Braunschweig, Germany.. cer@gbf.de
 SOURCE: Cytogenetic and genome research, (2003) Vol. 101, No. 1,

pp. 47-53.
Journal code: 101142708. E-ISSN: 1424-859X.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20031023
Last Updated on STN: 20040316
Entered Medline: 20040315

AB Tubulin tyrosine ligase (TTL) is a cytosolic enzyme involved in the posttranslational modification of tubulin. In the assembled form microtubules are detyrosinated over time at the C-terminus of alpha-tubulin. After microtubular disassembly TTL restores tyrosine residues back to the detyrosinated tubulin leading to a cycle of detyrosination/tyrosination. Here we report the isolation of the human and mouse TTL cDNA. In comparison with other known TTL sequences, namely bovine, rat and porcine, we found that only porcine TTL deviates in length by having an insertion of two glutamate residues. In mouse and human TTL the genomic coding sequence is composed of seven exons with normal intron/exon boundaries. Using fluorescence *in situ* hybridization (FISH), we mapped the murine TTL gene to mouse chromosome 2 (MMU2). Human TTL has been located to chromosome 2q13 (HSA2q13). In addition, we found frequently truncated PCR products of hTTL transcripts with aberrant splicing in tumors.

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L8 ANSWER 24 OF 39 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2003006942 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12512949
TITLE: Cloning of rat olfactory bulb tubulin tyrosine ligase cDNA: a dominant negative mutant and an antisense cDNA increase the proliferation rate of cells in culture.
AUTHOR: Mas Carlos R; Arregui Carlos O; Filiberti Adrian; Argarana Carlos E; Barra Hector S
CORPORATE SOURCE: Centro de Investigaciones en Quimica Biologica de Cordoba, CIQUIBIC (UNC-CONICET), Facultad de Ciencias Quimicas, Universidad Nacional de Cordoba, Cordoba, Argentina.
SOURCE: Neurochemical research, (2002 Nov) Vol. 27, No. 11, pp. 1453-8.
Journal code: 7613461. ISSN: 0364-3190.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030107
Last Updated on STN: 20030308
Entered Medline: 20030307

AB In this paper we describe the cloning of rat olfactory bulb tubulin tyrosine ligase (TTL) cDNA, and investigate the physiological role of TTL in cultured CHO-K1 cells. Comparison of the deduced amino acid sequence of rat TTL cDNA with those of bovine and pig showed approximately 90% of identity. Transient transfection of CHO-K1 cells with a dominant negative mutant of TTL that contains the binding site to the substrate (tubulin) but not the catalytic domain, significantly decreased the endogenous TTL activity as determined *in vitro*. Similar results were obtained using a construction encoding for the antisense sequence of TTL. The reduction in TTL activity is not accompanied by a decrease in the tyrosination levels of microtubules, as judged by immunofluorescence analysis. Strikingly, the number of cells in the plates transfected with the mutant TTL or the antisense TTL cDNA was, after 72 h of culture, two and three times higher, respectively, than the

number of cells in the control plates. These results support the hypothesis that TTL may play a role in the regulation of the cell cycle in living cells.

L8 ANSWER 25 OF 39 MEDLINE on STN DUPLICATE .7
ACCESSION NUMBER: 2001013397 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11004583
TITLE: Incorporation of nitrotyrosine into alpha-tubulin by recombinant mammalian tubulin-tyrosine ligase.
AUTHOR: Kalisz H M; Erck C; Plessmann U; Wehland J
CORPORATE SOURCE: Gesellschaft fur Biotechnologische Forschung, Abteilung Zellbiologie, Braunschweig, Germany.
SOURCE: Biochimica et biophysica acta, (2000 Aug 31) Vol. 1481, No. 1, pp. 131-8.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001102

AB Tubulin-tyrosine ligase (TTL, EC 6.3.2.25) from porcine brain, which catalyses the readdition of tyrosine to the C-terminus of detyrosinated alpha-tubulin, was cloned and expressed in Escherichia coli as a glutathione S-transferase-fusion protein. Upon cleavage of the immobilised fusion protein, an electrophoretically homogeneous enzyme was obtained. Recombinant TTL, which exhibited similar catalytic properties as the mammalian enzyme purified from brain tissue, was capable of using nitrotyrosine as an alternative substrate in vitro. Incorporation of tyrosine into tubulin was competitively inhibited by nitrotyrosine with an apparent K(i) of 0.24 mM. The TTL-catalysed incorporation of nitrotyrosine as sole substrate into alpha-tubulin was clearly detectable at concentrations of 10 microM by immunological methods using nitrotyrosine specific antibodies. However, in competition with tyrosine 20-fold higher concentrations of nitrotyrosine were necessary before its incorporation became evident. Analysis of the C-terminal peptides of in vitro modified alpha-tubulin by MALDI-MS confirmed the covalent incorporation of nitrotyrosine into tubulin by TTL. In contrast to the C-terminal tyrosine, pancreatic carboxypeptidase A was incapable of cleaving nitrotyrosine from the modified alpha-tubulin.

L8 ANSWER 26 OF 39 MEDLINE on STN DUPLICATE .8
ACCESSION NUMBER: 2001070000 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11054573
TITLE: Characterization of the human tubulin tyrosine ligase-like 1 gene (TTLL1) mapping to 22q13.1.
AUTHOR: Trichet V; Ruault M; Roizes G; De Sario A
CORPORATE SOURCE: Sequences Repetees et Centromeres Humains, CNRS UPR 1142, Institut de Biologie, 4, bv Henri IV, 34060, Montpellier, France.
SOURCE: Gene, (2000 Oct 17) Vol. 257, No. 1, pp. 109-17.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF104927; GENBANK-AF173935
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322
Entered Medline: 20010104

AB This paper reports the characterization of the human tubulin tyrosine ligase-like 1 gene (TTLL1), which maps to the chromosome region 22q13.1 and has been partially duplicated on three other acrocentric chromosomes: 13, 15 and 21. We describe the complete cDNA, TTLL1a, coding for the putative 423 amino acid long TTLL1 and alternative transcripts coding for truncated TTLL1. Likely TTLL1a corresponds to the 1.8 kb transcript that was detected in a wide range of tissues and has a stronger expression in heart, brain and testis. A 4.8 kb transcript was found only in brain tissues. We present an interspecies sequence comparison, revealing three conserved domains, named TTLD1, TTLD2 and TTLD3, that are specific to the TTLs and TTL-like proteins.

L8 ANSWER 27 OF 39 MEDLINE on STN
ACCESSION NUMBER: 2000148025 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10685598
TITLE: Tubulin-tyrosine ligase, a long-lasting enigma.
AUTHOR: Erck C; Frank R; Wehland J
CORPORATE SOURCE: Abteilung Zellbiologie, Gesellschaft fuer Biotechnologische Forschung, Braunschweig, Germany.
SOURCE: Neurochemical research, (2000 Jan) Vol. 25, No. 1, pp. 5-10. Ref: 48
Journal code: 7613461. ISSN: 0364-3190.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000309

AB Tubulins and microtubules are subjected to several post-translational modifications of which the reversible detyrosination/tyrosination of the carboxy-terminal end of most alpha-tubulins has been extensively analysed. This modification cycle involves a specific carboxypeptidase and the activity of the tubulin-tyrosine ligase (TTL). The true physiological function of TTL has so far not been established. This review describes the purification of TTL to homogeneity by biochemical methods, its in vitro properties and the generation of monoclonal antibodies. These mabs not only enabled a very convenient and rapid purification of TTL by immunoaffinity chromatography but also its extensive characterization by protein sequencing, which led to the isolation of the full length cDNA. With this information, gene disruption should be feasible in order to determine the physiological significance of the tyrosination cycle.

L8 ANSWER 28 OF 39 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:434745 SCISEARCH
THE GENUINE ARTICLE: 321LD
TITLE: Phosphorylation of tubulin tyrosine ligase: A potential mechanism for regulation of alpha-tubulin tyrosination
AUTHOR: Idriss H T (Reprint)
CORPORATE SOURCE: Univ St Andrews, Sch Biomed Sci, N Haugh, St Andrews KY16 9ST, Fife, Scotland (Reprint); Univ St Andrews, Ctr Biomed Sci, St Andrews KY16 9ST, Fife, Scotland; Univ Texas, Med Branch, Sealy Ctr Mol Sci, Galveston, TX 77550 USA
COUNTRY OF AUTHOR: Scotland; USA
SOURCE: CELL MOTILITY AND THE CYTOSKELETON, (MAY 2000) Vol. 46, No. 1, pp. 1-5.

PUBLISHER: ISSN: 0886-1544.
WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW
YORK, NY 10158-0012 USA.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 28
ENTRY DATE: Entered STN: 2000
Last Updated on STN: 2000

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The tubulin tyrosination/detyrosination cycle is a well-established posttranslational modification, which is carried out by two enzymes: Tubulin Tyrosine Ligase (TTL) and Tubulin Tyrosine Carboxypeptidase (TTCP). In this paper, I present evidence suggesting that the cycle itself is under the hierarchical control of reversible phosphorylation and that PKC mediated phosphorylation of TTL inhibits its activity, thereby preventing tubulin tyrosination. Phosphorylation of TTL is predicted to occur in a postulated Mg++/-ATP binding fold, leading to inhibition of Mg++/ATP binding and TTL mediated catalysis. The implications of such control are also discussed. (C) 2000 Wiley-Liss, Inc.

L8 ANSWER 29 OF 39 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1998070560 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9405300
TITLE: Suppression of tubulin tyrosine ligase during tumor growth.
AUTHOR: Lafanechere L; Courtay-Cahen C; Kawakami T; Jacrot M;
Rudiger M; Wehland J; Job D; Margolis R L
CORPORATE SOURCE: Laboratoire du Cytosquelette, INSERM U366, DBMS,
Commisariat a l'Energie Atomique/Grenoble, Grenoble,
France.
SOURCE: Journal of cell science, (1998 Jan) Vol. 111 (Pt 2), pp.
171-81.
Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980326
Last Updated on STN: 19980326
Entered Medline: 19980317

AB The C terminus of the tubulin alpha-subunit of most eukaryotic cells undergoes a cycle of tyrosination and detyrosination using two specific enzymes, a tubulin tyrosine ligase (TTL) and a tubulin carboxypeptidase. Although this enzyme cycle is conserved in evolution and exhibits rapid turnover, the meaning of this modification has remained elusive. We have isolated several NIH-3T3 derived clonal cell lines that lack TTL (TTL-). TTL- cells contain a unique tubulin isotype (delta2-tubulin) that can be detected with specific antibodies. When injected into nude mice, both TTL- cells and TTL+ cells stably transfected with TTL cDNA form sarcomas. But in tumors formed from TTL rescued cells, TTL is systematically lost during tumor growth. A strong selection process has thus acted during tumor growth to suppress TTL activity. In accord with this result, we find suppression of TTL activity in the majority of human tumors assayed with delta2-tubulin antibody. We conclude there is a widespread loss of TTL activity during tumor growth *in situ*, suggesting that TTL activity may play a role in tumor cell regulation.

L8 ANSWER 30 OF 39 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 97234553 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9118990
TITLE: Tubulin post-translational modifications--enzymes and their

AUTHOR: mechanisms of action.
MacRae T H
CORPORATE SOURCE: Department of Biology, Dalhousie University, Halifax,
Canada.
SOURCE: European journal of biochemistry / FEBS, (1997 Mar 1) Vol.
244, No. 2, pp. 265-78. Ref: 172
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 20000303
Entered Medline: 19970422

AB This review describes the enzymes responsible for the post-translational modifications of tubulin, including detyrosination/tyrosination, acetylation/deacetylation, phosphorylation, polyglutamylolation, polyglycylation and the generation of non-tyrosinatable alpha-tubulin. **Tubulin tyrosine-ligase**, which reattaches tyrosine to detyrosinated tubulin, has been extensively characterized and its gene sequenced. Enzymes such as tubulin-specific carboxypeptidase and alpha-tubulin acetyltransferase, required, respectively, for detyrosination and acetylation of tubulin, have yet to be purified to homogeneity and examined in defined systems. This has produced some conflicting results, especially for the carboxypeptidase. The phosphorylation of tubulin by several different types of kinases has been studied in detail but drawing conclusions is difficult because many of these enzymes modify proteins other than their actual substrates, an especially pertinent consideration for *in vitro* experiments. Tubulin phosphorylation in cultured neuronal cells has proven to be the best model for evaluation of kinase effects on tubulin/microtubule function. There is little information on the enzymes required for polyglutamylolation, polyglycylation, and production of non-tyrosinatable tubulin, but the available data permit interesting speculation of a mechanistic nature. Clearly, to achieve a full appreciation of tubulin post-translational changes the responsible enzymes must be characterized. Knowing when the enzymes are active in cells, if soluble or polymerized tubulin is the preferred substrate and the amino acid residues modified by each enzyme are all important. Moreover, acquisition of purified enzymes will lead to cloning and sequencing of their genes. With this information, one can manipulate cell genomes in order to either modify key enzymes or change their relative amounts, and perhaps reveal the physiological significance of tubulin post-translational modifications.

L8 ANSWER 31 OF 39 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 97261916 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9108330
TITLE: **Tubulin tyrosine ligase:**
protein and mRNA expression in developing rat skeletal muscle.
AUTHOR: Arregui C O; Mas C R; Argarana C E; Barra H S
CORPORATE SOURCE: Centro de Investigaciones en Quimica Biologica de Cordoba (CIQUIBIC), UNC-CONICET, Dpto. de Quimica Biologica, Facultad de Ciencias Quimicas, Universidad Nacional de Cordoba, Argentina.
SOURCE: Development, growth & differentiation, (1997 Apr) Vol. 39, No. 2, pp. 167-78.
Journal code: 0356504. ISSN: 0012-1592.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-U53214
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 20020212
Entered Medline: 19970724

AB Alpha tubulin can be post-translationally tyrosinated at the carboxy-terminus by a specific enzyme: tubulin tyrosine ligase. The expression of tubulin tyrosine ligase mRNA and protein during the development of rat skeletal muscle was examined in the present study. A portion of the coding region of the rat ligase cDNA was isolated and sequenced. The nucleotide and amino acid sequences showed about 90% homology with previously reported porcine and bovine ligase sequences. In newborn rats, ligase mRNA and protein were highly expressed in skeletal muscle. During early postnatal development, however, both ligase mRNA and protein dropped down dramatically. Quantitative measurements revealed that ligase protein at postnatal day 20 represented only 10% or less of the level at postnatal day 1. Ligase mRNA expression was also examined during the myogenesis in vitro. A strong ligase mRNA signal was detected in both undifferentiated myoblasts and cross-striated, contractile myotubes. The present results suggest that, during muscle differentiation, ligase function may be regulated by the amount of available mRNA. The discrepancy in the ligase expression between the in vivo and in vitro myogenesis suggests that factors controlling the levels of mRNA in vivo are lost in vitro.

L8 ANSWER 32 OF 39 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 93147125 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8093886
TITLE: Characterization of the tubulin-tyrosine ligase.
AUTHOR: Ersfeld K; Wehland J; Plessmann U; Dodemont H; Gerke V; Weber K
CORPORATE SOURCE: Max-Planck-Institute for Biophysical Chemistry, Department of Biochemistry, Goettingen, Germany.
SOURCE: The Journal of cell biology, (1993 Feb) Vol. 120, No. 3, pp. 725-32.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X68453
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 19930312
Last Updated on STN: 19980206
Entered Medline: 19930302

AB The sequence of tubulin-tyrosine ligase (TTL), the enzyme catalyzing the ATP-dependent posttranslational addition of a tyrosine to the carboxyterminal end of detyrosinated alpha-tubulin, has been determined. TTL from bovine and porcine brain was purified by immunoaffinity chromatography and extensively characterized by protein sequencing. Oligonucleotides derived from the protein sequence were synthesized and partial cDNA sequences were obtained using reversed transcribed brain mRNA in polymerase chain reactions. Polymerase chain reaction fragments were used to isolate a full-length cDNA clone from a randomly primed lambda gt10 cDNA library obtained from embryonic porcine brain mRNA. Porcine TTL is encoded by 1,137 nucleotides corresponding to 379 amino acid residues. It has a molecular weight of 43,425 and a calculated isoelectric point of 6.51. Northern blot analysis revealed a surprisingly long mRNA (approximately 6 kb in embryonic porcine brain). The protein sequence of TTL shares no extended homology with the sequences in the data banks. TTL contains a potential serine phosphorylation site for cAMP-dependent protein kinase (RKAS at positions

73 to 76). Residues 244 to 258 lie at the surface of the molecule. A rabbit antibody raised against a synthetic peptide corresponding to this sequence binds to native TTL. The same sequence contains the cleavage site for endoproteinase Glu-C (residue 248) previously shown to convert TTL into a nicked derivative in which the two fragments still form a tight complex but don't display enzymatic activity.

L8 ANSWER 33 OF 39 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1992:70844 SCISEARCH

THE GENUINE ARTICLE: HA993

TITLE: POLYGLUTAMYLATED ALPHA-TUBULIN CAN ENTER THE TYROSINATION DETYROSINATION CYCLE

AUTHOR: EDDIE B (Reprint); ROSSIER J; LECAER J P; PROME J C; DESBRUYERES E; GROS F; DENOULET P

CORPORATE SOURCE: COLL FRANCE, BIOCHIM CELLULAIRE LAB, 11 PL MARCELIN BERTHELOT, F-75231 PARIS 05, FRANCE (Reprint); CNRS, CTR RECH BIOCHIM & GENET CELLULAIRE, F-31062 TOULOUSE, FRANCE; CNRS, PHYSIOL NERVEUSE LAB, F-91198 GIF SUR YVETTE, FRANCE

COUNTRY OF AUTHOR: FRANCE

SOURCE: BIOCHEMISTRY, (21 JAN 1992) Vol. 31, No. 2, pp. 403-410. ISSN: 0006-2960.

PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 43

ENTRY DATE: Entered STN: 1994

Last Updated on STN: 1994

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have previously identified a major modification of neuronal alpha-tubulin which consists of the posttranslational addition of a varying number of glutamyl units on the gamma-carboxyl group of glutamate residue 445. This modification, called polyglutamylation, was initially found associated with detyrosinated alpha-tubulin [Eddé, B., Rossier, J., Le Caer, J. P., Desbruyères, E., Gros, F., & Denoulet, P. (1990) Science 247, 83-85]. In this report we show that a lateral chain of glutamyl units can also be present on tyrosinated alpha-tubulin. Incubation of cultured mouse brain neurons with radioactive tyrosine, in the presence of cycloheximide, resulted in a posttranslational labeling of six alpha-tubulin isoelectric variants. Because both tyrosination and polyglutamylation occur in the C-terminal region of alpha-tubulin, the structure of this region was investigated. [³H]tyrosinated tubulin was mixed with a large excess of unlabeled mouse brain tubulin and digested with thermolysin. Five peptides, detected by their radioactivity, were purified by high-performance liquid chromatography. Amino acid sequencing and mass spectrometry showed that one of these peptides corresponds to the native C-terminal part of alpha-tubulin (VEGESEESEEY)-V-440-Y-451 and that the remainders bear a varying number of glutamyl units linked to glutamate residue 445, which explains the observed heterogeneity of tyrosinated alpha-tubulin. A quantitative analysis showed that the different tyrosinated forms of alpha-tubulin represent a minor (13%) fraction of the total alpha-tubulin present in the brain and that most (80%) of these tyrosinated forms are polyglutamylated. The different forms of alpha-tubulin were found to be equal substrates for tubulin tyrosine ligase and tubulin carboxypeptidase, which indicates that alpha-tubulin can enter the tyrosination/detyrosination cycle independently of its degree of glutamylation.

L8 ANSWER 34 OF 39 MEDLINE on STN

ACCESSION NUMBER: 89150728 MEDLINE

DOCUMENT NUMBER: PubMed ID: 3067795

TITLE: Tubulin expression in trypanosomes..

AUTHOR: Gallo J M; Precigout E
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire, URA CNRS 80, UFR Sciences, Poitiers, France.
SOURCE: Biology of the cell / under the auspices of the European Cell Biology Organization, (1988) Vol. 64, No. 2, pp. 137-43. Ref: 46
Journal code: 8108529. ISSN: 0248-4900.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198904
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19900306
Entered Medline: 19890418

AB Microtubules in trypanosomes are the main component of the flagellar axoneme and of the subpellicular microtubule corset, whose relative positions determine the morphology of each cell stage of the life cycle of these parasites. Microtubules are polymers of tubulin, a protein dimer of two 55-kDa subunits, alpha- and beta-tubulin; in *Trypanosoma brucei*, the tubulin-coding sequences are clustered in a 40-kb fragment of tandemly repeated alpha- and beta-tubulin genes separated by a 170-bp intergenic zone. This cluster is transcribed in a unique RNA which is rapidly processed into mature mRNAs carrying the 5' 35-nucleotide leader sequence found in all trypanosome mRNAs. Although no heterogeneity has been found at the gene level, tubulin can be post-translationally modified in 2 ways: the C-terminal tyrosine of alpha-tubulin can be selectively cleaved and added again with 2 enzymes, tubulin carboxypeptidase and tubulin-tyrosine ligase; alpha-tubulin can also be acetylated on a lysine residue. Some molecular domains of tubulin are restricted to subpopulations of microtubules; for instance, the beta-tubulin form defined by the monoclonal antibody 1B41 is sequestered into a part of the subpellicular cytoskeleton limited to the flagellar adhesion zone, which might correspond to the group of 4 microtubules associated with a cisterna of the endoplasmic reticulum, forming the so-called "subpellicular microtubule quartet" (SFMQ). The early assembly of this zone in each daughter cell during the cell division of *T. brucei*, together with the alterations undergone by the domain defined by the monoclonal antitubulin 24E3 during the differentiation of *Trypanosoma cruzi*, suggest that specific tubulin forms are responsible for dynamic properties of SFMQ possibly involved in trypanosome morphogenesis.

L8 ANSWER 35 OF 39 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. ON STN
ACCESSION NUMBER: 1987-09146 BIOTECHDS
TITLE: Tubulin-tyrosine-ligase has a binding site on beta-tubulin: a 2-domain structure of the enzyme; hybridoma construction for monoclonal antibody production
AUTHOR: Wehland J; Weber K
CORPORATE SOURCE: Max-Planck-Inst.Biophys.Chem.
LOCATION: Max Planck Institute for Biophysical Chemistry, D-3400 Goettingen, Germany
SOURCE: J.Cell Biol.; (1987) 104, 4, 1059-67
CODEN: JCLBA3
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using 2 distinct tubulin-tyrosine-ligase monoclonal antibodies, several subunit-specific tubulin monoclonal antibodies, and chemical crosslinking, a ligase binding site was identified on beta-tubulin. For production of the enzyme specific antibodies, 6-wk-old female BALB/c mice were immunized 3 times at 3 wk intervals with 100-200 ug affinity purified ligase emulsified in Freund's complete adjuvant for the first injection and Freund's incomplete

adjuvant for the subsequent injections. The mice were tested for monoclonal antibody production, and spleen cells from the mouse with highest serum titer were fused with PAI myeloma cells. Positive producing hybridomas were cloned twice by limiting dilution and monoclonal antibodies produced in ascites fluid in BALB/c mice. The binding site characterized is retained when the carboxy-terminal domains of both tubulin subunits are removed by subtilisin treatment. This explains the extreme substrate specificity of the enzyme, which does not act on other cellular proteins or carboxy-terminal peptides derived from detyrosinated alpha-tubulin. (42 ref)

L8 ANSWER 36 OF 39 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1985-04125 BIOTECHDS
TITLE: Purification of brain tubulin-tyrosine-ligase by biochemical and immunological methods; monoclonal antibody preparation and hybridoma construction
AUTHOR: Schroeder H C; Wehland J; Weber K
CORPORATE SOURCE: Max-Planck-Inst.Biophys.Chem.
LOCATION: Institute for Physiological Chemistry, University of Mainz, D-6500 Mainz, Germany.
SOURCE: J.Cell Biol.; (1985) 100, 1, 276-81
CODEN: JCLBA3
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tubulin-tyrosin-ligase (TTL) was purified biochemically from pig brain tissue to near homogeneity (over 95%). The purified enzyme, (10-20 ug) was then injected 3 times into Balb/c mice at intervals of 3 weeks. Freund's complete adjuvant and incomplete adjuvant were used for the first and last 2 injections respectively. Immune spleen cells were fused with PAI myeloma cells, and hybridomas were selected in HAT. Those secreting monoclonal antibody to TTL were cloned twice in soft agar. The antibodies specifically recognized TTL in brain and liver tissue of various mammals. Purified ascites IgG were coupled to CNBr-activated Sepharose 4B. TTL from crude brain extract selectively bound to this immunoaffinity column in 1.5 M NaCl and eluted with 3 M NaCl. The purity of the eluted TTL was over 95%. It was a monomeric protein of apparent mol.weight 40,000. It associated as a 1/1 complex with alpha-beta-tubulin on gradient centrifugation. (32 ref)

L8 ANSWER 37 OF 39 MEDLINE on STN
ACCESSION NUMBER: 84180758 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6201294
TITLE: Organization of microtubules in stabilized meristematic plant cells revealed by a rat monoclonal antibody reacting only with the tyrosinated form of alpha-tubulin.
AUTHOR: Wehland J; Schroeder M; Weber K
SOURCE: Cell biology international reports, (1984 Feb) Vol. 8, No. 2, pp. 147-50.
Journal code: 7708050. ISSN: 0309-1651.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198406
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19840619

AB A rat monoclonal antibody against yeast tubulin (clone YL 1/2; Kilmartin et al., 1982) that reacts specifically with mammalian alpha-tubulin carrying a carboxyterminal tyrosine residue (Wehland et al., 1983) was used to localize microtubules in plant cells derived from onion root apices (*Allium cepa L.*). YL 1/2 reacted with all types of microtubular arrays known to occur in higher plant meristematic cells such as interphase cortical microtubules, pre-prophase bands, the mitotic

spindle and phragmoplast microtubules. The specific labeling of microtubules in isolated cells from onion root tips by YL 1/2 indicates that plant cells like animal cells contain tubulin tyrosine ligase, the enzyme which posttranslationally modifies alpha-tubulin. This enzyme could be involved in the dynamic regulation of microtubular arrays in all eukaryotic cells.

L8 ANSWER 38 OF 39 HCPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:81418 HCPLUS
DOCUMENT NUMBER: 100:81418
TITLE: State of tyrosination of soluble synaptosomal tubulin
AUTHOR(S): Barra, Hector S.; Arce, Carlos A.
CORPORATE SOURCE: Fac. Cienc. Quim., UNC, Cordoba, 5016, Argent.
SOURCE: Comunicaciones Biologicas (1983), 2(1), 13-18
CODEN: COBIEJ; ISSN: 0326-1956
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The presence of tubulin-tyrosine ligase and the state of tyrosination of tubulin in the soluble synaptosomal fraction from rat brain was studied. The ligase was present in this soluble fraction and the amts. of tyrosinated and nontyrosinated tubulin (expressed as nmol/mg protein) were similar to those in the cytosolic fraction.

L8 ANSWER 39 OF 39 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 79099794 EMBASE
DOCUMENT NUMBER: 1979099794
TITLE: Studies on NGF induced differentiation in PC12 pheochromocytoma cells. Specific rise in tyrosyl tubulin ligase activity induced by the nerve growth factor.
AUTHOR: Levi A.; Castellani L.; Calissano P.; et al.
CORPORATE SOURCE: Lab. Biol. Cell., CNR, Roma, Italy
SOURCE: Bulletin of Molecular Biology and Medicine, (1978) Vol. 3, No. SUPPL. 1, pp. 42s-50s.
CODEN: BMBMD5
COUNTRY: Italy
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
003 Endocrinology
029 Clinical Biochemistry
030 Pharmacology
LANGUAGE: English

AB A model system for the in vitro study of the mechanism of action of nerve growth factor (NGF) is described. The PC12 clonal line derived from a rat pheochromocytoma is shown to be very similar to the stem cell progenitor of both adrenal cromaffin cells and sympathetic neurones and to differentiate morphologically and physiologically like a nerve cell in response to NGF. Studies on tyrosyl tubulin ligase activity as a function of NGF induced differentiation in PC12 cells are reported.

=> d his

(FILE 'HOME' ENTERED AT 12:08:31 ON 28 FEB 2006)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCPLUS, NTIS, LIFESCI' ENTERED AT 12:09:07 ON 28 FEB 2006

L1 7010 S TESTIS (W) SPECIFIC
L2 431 S TYROSINE (W)LIGASE?
L3 3 S L1 AND L2
L4 2 DUP REM L3 (1 DUPLICATE REMOVED)
L5 405 S TUBULIN (A) L2
L6 7556238 S CLON? OR EXPRESS? OR RECOMBINANT
L7 83 S L5 AND L6

L8 39 DUP REM L7 (44 DUPLICATES REMOVED)

=> s 18 and testis
L9 8 L8 AND TESTIS

=> d 1-8 ibib ab

L9 ANSWER 1 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2001070000 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11054573
TITLE: Characterization of the human tubulin tyrosine ligase-like 1 gene (TTLL1) mapping to 22q13.1.
AUTHOR: Trichet V; Ruault M; Roizes G; De Sario A
CORPORATE SOURCE: Sequences Repetees et Centromeres Humains, CNRS UPR 1142, Institut de Biologie, 4, bv Henri IV, 34060, Montpellier, France.
SOURCE: Gene, (2000 Oct 17) Vol. 257, No. 1, pp. 109-17.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF104927; GENBANK-AF173935
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010104

AB This paper reports the characterization of the human tubulin tyrosine ligase-like 1 gene (TTLL1), which maps to the chromosome region 22q13.1 and has been partially duplicated on three other acrocentric chromosomes: 13, 15 and 21. We describe the complete cDNA, TTLL1a, coding for the putative 423 amino acid long TTLL1 and alternative transcripts coding for truncated TTLL1. Likely TTLL1a corresponds to the 1.8 kb transcript that was detected in a wide range of tissues and has a stronger expression in heart, brain and testis. A 4.8 kb transcript was found only in brain tissues. We present an interspecies sequence comparison, revealing three conserved domains, named TTLD1, TTLD2 and TTLD3, that are specific to the TTLs and TTL-like proteins.

L9 ANSWER 2 OF 8 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-07314 BIOTECHDS
TITLE: New testis-specific tubulin tyrosine-ligase-like BGS-42 polypeptide, useful for preventing, treating or ameliorating a medical condition, e.g. aberrant cellular proliferation, reproductive disorders or testicular disorders; involving vector-mediated gene transfer, expression in host cell for use in gene therapy

AUTHOR: FEDER J N; WU S; NELSON T C
PATENT ASSIGNEE: BRISTOL-MYERS SQUIBB CO
PATENT INFO: WO 2004005487 15 Jan 2004
APPLICATION INFO: WO 2003-US21605 9 Jul 2003
PRIORITY INFO: US 2002-394725 9 Jul 2002; US 2002-394725 9 Jul 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-099381 [10]

AB DERWENT ABSTRACT:
NOVELTY - A testis-specific tubulin tyrosine-ligase-like polypeptide, designated BGS-42 polypeptide, is new.

DETAILED DESCRIPTION - A testis-specific tubulin tyrosine-ligase-like polypeptide, designated BGS-42 polypeptide comprises or consists of:(a) a polypeptide fragment, domain,

epitope or the full-length protein of a fully defined sequence of 541 amino acids (I), as given in the specification, or the encoded sequence included in ATCC Deposit Number PTA-4454, having tyrosine tubulin ligase activity; (b) a polypeptide comprising amino acids 2-541 of the sequence of (I), where the amino acids 2-541 comprises a polypeptide of (I) minus the start methionine; (c) a polypeptide comprising amino acids 1-541 or 73-365 of the sequence of (I); or (d) a polypeptide comprising at least 424 contiguous amino acids of the sequence of (I). INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid molecule comprising or consisting of: (a) a polynucleotide fragment of 1838 bp (II), fully defined in the specification, or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit Number PTA-4454, which is hybridizable to the sequence of (II); (b) a polynucleotide encoding a polypeptide fragment, domain, epitope or the full-length protein of the sequence of (I), or a polypeptide fragment, domain or epitope encoded by the cDNA sequence included in ATCC Deposit Number PTA-4454, which is hybridizable to the sequence of (II), having tyrosine tubulin ligase activity; (c) a polynucleotide which is a variant or an allelic variant of (II); (d) nucleotides 156-1775 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 2-541 of (I) minus the start methionine; (e) nucleotides 153-1775 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 1-541 of (I) including the start codon; (f) nucleotides 369-1247 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 73-365 of (I); (g) a polynucleotide that encodes at least 424 contiguous amino acids of (I); (h) at least 1272 contiguous nucleotides of (II); (i) a polynucleotide which represents the complementary sequence (antisense) of (II); (j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides above, where the polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A or only T residues; (k) a polynucleotide comprising or consisting of the BGS-42 gene or BGS-42 promoter; or (l) a nucleotide sequence of 2241 bp, fully defined in the specification; (2) a recombinant vector comprising the isolated nucleic acid molecule; (3) an isolated antibody that binds specifically to BGS-42 polypeptide; (4) a recombinant host cell comprising the vector sequences, or expressing the BGS-42 polypeptide; (5) making an isolated polypeptide; (6) preventing, treating or ameliorating a medical condition; and (7) diagnosing a pathological condition or a susceptibility to a pathological condition in a subject.

WIDER DISCLOSURE - Also disclosed are screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides, and methods of controlling the expression of the polypeptide.

BIOTECHNOLOGY - Preparation (claimed): The BGS-42 polypeptide is prepared by standard recombinant methods. Making an isolated polypeptide comprises culturing the recombinant host cell under conditions such that the polypeptide is expressed, and recovering the polypeptide. Preferred Polypeptide: The full-length protein comprises sequential amino acid deletions from the C-terminus or the N-terminus. Preferred Nucleic Acid: The polynucleotide fragment consists of a nucleotide sequence encoding a human tyrosine tubulin ligase. Preferred Method: Preventing, treating or ameliorating a medical condition comprises administering to a mammalian subject a therapeutic amount of the BGS-42 polypeptide or its modulator. Diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprises determining the presence or absence of a mutation in the polynucleotide cited above, and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of the mutation. Alternatively, the method comprises determining the presence or amount of expression of the BGS-42 polypeptide in a tyrosine tubulin ligase sample, and diagnosing a pathological condition or a susceptibility to a pathological condition based on the

presence or amount of expression of the polypeptide.

ACTIVITY - Cytostatic; Respiratory-Gen.; Gastrointestinal-Gen.; Neuroprotective; Endocrine-Gen.; Antiinflammatory; Anabolic; Hypertensive; Osteopathic; Nootropic; Antiparkinsonian; Antiarthritic; Antiasthmatic; Anti-HIV; Antibacterial; Immunosuppressive; Antiseborrheic; Dermatological. No biological data given.

MECHANISM OF ACTION - Tyrosine Ligase Modulator; Gene Therapy. No biological data given.

USE - The BGS-42 polypeptide or polynucleotide can be used for diagnosing a pathological condition or a susceptibility to a pathological condition in a subject, and for preventing, treating or ameliorating a medical condition, such as a disorder related to aberrant tubulin ligase activity, a disorder related to aberrant tubulin-carboxypeptidase activity, aberrant cellular proliferation, reproductive disorders, testicular disorders, testicular cancer, pulmonary disorders, lung cancer, gastrointestinal disorders, colon cancer, stomach cancer, neural disorders, brain cancer, liver cancer, or proliferative condition of the testis, lung, small intestine, brain or lymph tissue (all claimed). The BGS-42 polypeptide, polynucleotide, or their modulators are also useful for treating infertility, Cushing's syndrome, emphysema, pneumonia, Addison's disease, acromegaly, Alzheimer's disease, or Parkinson's disease. The BGS-42 polypeptide can be used as a preventive agent for immunological disorders including arthritis, asthma, AIDS, sepsis, acne, Sjogren's disease or scleroderma. The antibodies may be used to purify, detect and target the BGS-42 polypeptides.

ADMINISTRATION - Administration of the antibody is 0.1-100 (preferably 1-10) mg/kg, intradermally, intramuscularly, intraperitoneally, intravenously, subcutaneously, intranasally, epidurally, intraventricularly, intrathecally, topically, orally, or rectally.

EXAMPLE - A polynucleotide encoding a BGS-42 polypeptide was amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence to synthesize insertion fragments. The pQE-9 vector was digested with BamHI and XbaI and the amplified fragment was ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial ribosome-binding site. The ligation mixture was used to transform Escherichia coli strain M15/rep4. Transformants were identified by their ability to grow on LB (Luria bertani) plates, and ampicillin/kanamycin-resistant colonies were selected. Clones containing the desired constructs were grown overnight in liquid culture, i.e. LB media, supplemented with both ampicillin and kanamycin. Isopropyl-B-D-thiogalacto pyranoside (IPTG) was added to induce gene expression. Cells were grown for an extra 3-4 hours, and cells were harvested by centrifugation. The cell pellet obtained by centrifugation was solubilized, and the solubilized BGS-42 protein was purified using a metal chelating column under conditions that allow tight binding of the protein. (343 pages)

L9 ANSWER 3 OF 8 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:156681 HCPLUS
Correction of: 2005:60757

DOCUMENT NUMBER: 142:216629
Correction of: 142:132329

TITLE: Gene expression profiles and biomarkers for the detection of hyperlipidemia and other disease-related gene transcripts in blood

INVENTOR(S): Liew, Choong-Chin

PATENT ASSIGNEE(S): Chondrogene Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S.
Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 47

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004248170 | A1 | 20041209 | US 2004-812777 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004248170 | A1 | 20041209 | US 2004-812777 | 20040330 |
| US 2004248170 | A1 | 20041209 | US 2004-812777 | 20040330 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812777 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular hyperlipidemia, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

L9 ANSWER 4 OF 8 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:156228 HCPLUS
Correction of: 2005:16967

DOCUMENT NUMBER: 142:192331
Correction of: 142:108390

TITLE: Quantitative RT-PCR method for the detection in blood of microarray-identified rheumatoid arthritis-related gene transcripts for diagnosing and monitoring disease state

INVENTOR(S): Liew, Choong-Chin

PATENT ASSIGNEE(S): Chondrogene Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 81 pp., Cont.-in-part of U.S. Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 47

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2005003394 | A1 | 20050106 | US 2004-812782 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |

| | | | | |
|------------------------|----|----------|-----------------|-------------|
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| US 2005003394 | A1 | 20050106 | US 2004-812782 | 20040330 |
| US 2005003394 | A1 | 20050106 | US 2004-812782 | 20040330 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812782 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood for diagnosing and monitoring diseases. The present invention demonstrates that a simple drop of blood may be used to determine the quant. expression of various mRNAs that reflect the health/disease state of the subject through the use of quant. reverse transcription-polymerase chain reaction (QRT-PCR) anal. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring rheumatoid arthritis using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

L9 ANSWER 5 OF 8 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:60755 HCPLUS

Correction of: 2004:1036570

DOCUMENT NUMBER: 142:154259

Correction of: 142:36938

TITLE: Analysis of genetic information contained in peripheral blood for diagnosis, prognosis and monitoring treatment of allergy, infection and genetic disease in human

INVENTOR(S): Liew, Choong-Chin

PATENT ASSIGNEE(S): Chondrogene Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S. Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 47

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004241726 | A1 | 20041202 | US 2004-812707 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004241726 | A1 | 20041202 | US 2004-812707 | 20040330 |
| US 2004241726 | A1 | 20041202 | US 2004-812707 | 20040330 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812707 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular allergy, using gene-specific

and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.]

L9 ANSWER 6 OF 8 HCPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:60754 HCPLUS
 Correction of: 2004:1036571
 DOCUMENT NUMBER: 142:233342
 Correction of: 142:16836
 TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
 INVENTOR(S): Liew, Choong-Chin
 PATENT ASSIGNEE(S): Chondrogene Limited, Can.
 SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 47
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004241727 | A1 | 20041202 | US 2004-812731 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004241727 | A1 | 20041202 | US 2004-812731 | 20040330 |
| US 2004241727 | A1 | 20041202 | US 2004-812731 | 20040330 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| US 2005208519 | A1 | 20050922 | US 2004-989191 | 20041115 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812731 | A 20040330 |
| | | | WO 2004-US20836 | A2 20040621 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L9 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1997 HCAPLUS
 DOCUMENT NUMBER: 142:111841
 TITLE: Gene expression profiles and biomarkers for the detection of depression-related and other disease-related gene transcripts in blood
 INVENTOR(S): Liew, Choong-Chin
 PATENT ASSIGNEE(S): Chondrogene Limited, Can.
 SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 802,875.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 47
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004265868 | A1 | 20041230 | US 2004-812702 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | 20040330 |
| US 2004265868 | A1 | 20041230 | US 2004-812702 | 20040330 |
| US 2004265868 | A1 | 20041230 | US 2004-812702 | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-812702 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular mental depression, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

L9 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:722839 HCAPLUS
 DOCUMENT NUMBER: 141:238811
 TITLE: Protein and cDNA sequences of a novel human testis-specific tubulin tyrosine ligase like protein BGS-42, and diagnostic and therapeutic use
 INVENTOR(S): Feder, John N.; Nelson, Thomas C.; Wu, Shujian; Krystek, Stanley R.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 199 pp., Cont.-in-part of U.S. Ser. No. 615,659.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004171131 | A1 | 20040902 | US 2003-635977 | 20030807 |
| US 2004157234 | A1 | 20040812 | US 2003-615659 | 20030709 |
| PRIORITY APPLN. INFO.: | | | US 2002-394725P | P 20020709 |
| | | | US 2003-615659 | A2 20030709 |

AB The present invention provides novel polynucleotides encoding BGS-42 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel BGS-42 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

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| E2 | 74 | FEDER J M/AU |
| E3 | 185 --> | FEDER J N/AU |
| E4 | 1 | FEDER J N */AU |
| E5 | 16 | FEDER JACK B/AU |
| E6 | 1 | FEDER JAN DAVID/AU |
| E7 | 1 | FEDER JEAN M/AU |
| E8 | 3 | FEDER JEAN MARC/AU |
| E9 | 60 | FEDER JEFFREY L/AU |
| E10 | 88 | FEDER JENS/AU |
| E11 | 1 | FEDER JOHANN/AU |
| E12 | 2 | FEDER JOHANN G/AU |

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L10 185 "FEDER J N"/AU

=> e wu s/au

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| E4 | 1 | WU S */AU |
| E5 | 24 | WU S A/AU |
| E6 | 86 | WU S B/AU |
| E7 | 1667 | WU S C/AU |
| E8 | 1 | WU S C C/AU |
| E9 | 3 | WU S C G/AU |
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| E11 | 6 | WU S C S/AU |
| E12 | 1 | WU S C X P/AU |

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L11 3568 "WU S"/AU

=> e nelson t c/au

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| E7 | 50 | NELSON T F/AU |

E8 1 NELSON T F JR/AU
E9 38 NELSON T G/AU
E10 55 NELSON T H/AU
E11 12 NELSON T HOLLAND/AU
E12 2 NELSON T I/AU

=> s e3
L12 130 "NELSON T C"/AU

=> d his

(FILE 'HOME' ENTERED AT 12:08:31 ON 28 FEB 2006)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
LIFESCI' ENTERED AT 12:09:07 ON 28 FEB 2006

L1 7010 S TESTIS (W) SPECIFIC
L2 431 S TYROSINE (W)LIGASE?
L3 3 S L1 AND L2
L4 2 DUP REM L3 (1 DUPLICATE REMOVED)
L5 405 S TUBULIN (A) L2
L6 7556238 S CLON? OR EXPRESS? OR RECOMBINANT
L7 83 S L5 AND L6
L8 39 DUP REM L7 (44 DUPLICATES REMOVED)
L9 8 S L8 AND TESTIS
E FEDER J N/AU
L10 185 S E3
E WU S/AU
L11 3568 S E3
E NELSON T C/AU
L12 130 S E3

=> s l10 or l11 or l12
L13 3853 L10 OR L11 OR L12

=> s l2 and l13
L14 1 L2 AND L13

=> d all

L14 ANSWER 1 OF 1 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-07314 BIOTECHDS
TI New testis-specific tubulin tyrosine-ligase-like
BGS-42 polypeptide, useful for preventing, treating or ameliorating a
medical condition, e.g. aberrant cellular proliferation, reproductive
disorders or testicular disorders;
involving vector-mediated gene transfer, expression in host cell for
use in gene therapy
AU FEDER J N; WU S; NELSON T C
PA BRISTOL-MYERS SQUIBB CO
PI WO 2004005487 15 Jan 2004
AI WO 2003-US21605 9 Jul 2003
PRAI US 2002-394725 9 Jul 2002; US 2002-394725 9 Jul 2002
DT Patent
LA English
OS WPI: 2004-099381 [10]
AB DERVENT ABSTRACT:
NOVELTY - A testis-specific tubulin tyrosine-ligase
-like polypeptide, designated BGS-42 polypeptide, is new.
DETAILED DESCRIPTION - A testis-specific tubulin tyrosine-
ligase-like polypeptide, designated BGS-42 polypeptide comprises
or consists of: (a) a polypeptide fragment, domain, epitope or the
full-length protein of a fully defined sequence of 541 amino acids (I),
as given in the specification, or the encoded sequence included in ATCC
Deposit Number PTA-4454, having tyrosine tubulin ligase activity; (b) a

polypeptide comprising amino acids 2-541 of the sequence of (I), where the amino acids 2-541 comprises a polypeptide of (I) minus the start methionine; (c) a polypeptide comprising amino acids 1-541 or 73-365 of the sequence of (I); or (d) a polypeptide comprising at least 424 contiguous amino acids of the sequence of (I). INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid molecule comprising or consisting of: (a) a polynucleotide fragment of 1838 bp (II), fully defined in the specification, or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit Number PTA-4454, which is hybridizable to the sequence of (II); (b) a polynucleotide encoding a polypeptide fragment, domain, epitope or the full-length protein of the sequence of (I), or a polypeptide fragment, domain or epitope encoded by the cDNA sequence included in ATCC Deposit Number PTA-4454, which is hybridizable to the sequence of (II), having tyrosine tubulin ligase activity; (c) a polynucleotide which is a variant or an allelic variant of (II); (d) nucleotides 156-1775 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 2-541 of (I) minus the start methionine; (e) nucleotides 153-1775 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 1-541 of (I) including the start codon; (f) nucleotides 369-1247 of the sequence of (II), where the nucleotides encode a polypeptide corresponding to amino acids 73-365 of (I); (g) a polynucleotide that encodes at least 424 contiguous amino acids of (I); (h) at least 1272 contiguous nucleotides of (II); (i) a polynucleotide which represents the complementary sequence (antisense) of (II); (j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides above, where the polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A or only T residues; (k) a polynucleotide comprising or consisting of the BGS-42 gene or BGS-42 promoter; or (l) a nucleotide sequence of 2241 bp, fully defined in the specification; (2) a recombinant vector comprising the isolated nucleic acid molecule; (3) an isolated antibody that binds specifically to BGS-42 polypeptide; (4) a recombinant host cell comprising the vector sequences, or expressing the BGS-42 polypeptide; (5) making an isolated polypeptide; (6) preventing, treating or ameliorating a medical condition; and (7) diagnosing a pathological condition or a susceptibility to a pathological condition in a subject.

WIDER DISCLOSURE - Also disclosed are screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides, and methods of controlling the expression of the polypeptide.

BIOTECHNOLOGY - Preparation (claimed): The BGS-42 polypeptide is prepared by standard recombinant methods. Making an isolated polypeptide comprises culturing the recombinant host cell under conditions such that the polypeptide is expressed, and recovering the polypeptide. Preferred Polypeptide: The full-length protein comprises sequential amino acid deletions from the C-terminus or the N-terminus. Preferred Nucleic Acid: The polynucleotide fragment consists of a nucleotide sequence encoding a human tyrosine tubulin ligase. Preferred Method: Preventing, treating or ameliorating a medical condition comprises administering to a mammalian subject a therapeutic amount of the BGS-42 polypeptide or its modulator. Diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprises determining the presence or absence of a mutation in the polynucleotide cited above, and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of the mutation. Alternatively, the method comprises determining the presence or amount of expression of the BGS-42 polypeptide in a tyrosine tubulin ligase sample, and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

ACTIVITY - Cytostatic; Respiratory-Gen.; Gastrointestinal-Gen.; Neuroprotective; Endocrine-Gen.; Antiinflammatory; Anabolic; Hypertensive; Osteopathic; Nootropic; Antiparkinsonian; Antiarthritic;

Antiasthmatic; Anti-HIV; Antibacterial; Immunosuppressive;
Antiseborrheic; Dermatological. No biological data given.

MECHANISM OF ACTION - Tyrosine Ligase Modulator;
Gene Therapy. No biological data given.

USE - The BGS-42 polypeptide or polynucleotide can be used for diagnosing a pathological condition or a susceptibility to a pathological condition in a subject, and for preventing, treating or ameliorating a medical condition, such as a disorder related to aberrant tubulin ligase activity, a disorder related to aberrant tubulin-carboxypeptidase activity, aberrant cellular proliferation, reproductive disorders, testicular disorders, testicular cancer, pulmonary disorders, lung cancer, gastrointestinal disorders, colon cancer, stomach cancer, neural disorders, brain cancer, liver cancer, or proliferative condition of the testis, lung, small intestine, brain or lymph tissue (all claimed). The BGS-42 polypeptide, polynucleotide, or their modulators are also useful for treating infertility, Cushing's syndrome, emphysema, pneumonia, Addison's disease, acromegaly, Alzheimer's disease, or Parkinson's disease. The BGS-42 polypeptide can be used as a preventive agent for immunological disorders including arthritis, asthma, AIDS, sepsis, acne, Sjogren's disease or scleroderma. The antibodies may be used to purify, detect and target the BGS-42 polypeptides.

ADMINISTRATION - Administration of the antibody is 0.1-100 (preferably 1-10) mg/kg, intradermally, intramuscularly, intraperitoneally, intravenously, subcutaneously, intranasally, epidurally, intraventricularly, intrathecally, topically, orally, or rectally.

EXAMPLE - A polynucleotide encoding a BGS-42 polypeptide was amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence to synthesize insertion fragments. The pQE-9 vector was digested with BamHI and XbaI and the amplified fragment was ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial ribosome-binding site. The ligation mixture was used to transform Escherichia coli strain M15/rep4. Transformants were identified by their ability to grow on LB (Luria bertani) plates, and ampicillin/kanamycin-resistant colonies were selected. Clones containing the desired constructs were grown overnight in liquid culture, i.e. LB media, supplemented with both ampicillin and kanamycin. Isopropyl-B-D-thiogalacto pyranoside (IPTG) was added to induce gene expression. Cells were grown for an extra 3-4 hours, and cells were harvested by centrifugation. The cell pellet obtained by centrifugation was solubilized, and the solubilized BGS-42 protein was purified using a metal chelating column under conditions that allow tight binding of the protein. (343 pages)

CC THERAPEUTICS, Protein Therapeutics; GENETIC TECHNIQUES and APPLICATIONS, Gene Expression Techniques and Analysis; DISEASE, Cancer; DISEASE, Central Nervous System; DISEASE, HIV and Other Virus Infections; DISEASE, Other Diseases; DIAGNOSTICS, Molecular Diagnostics; THERAPEUTICS, Gene Therapy

CT RECOMBINANT TESTIS-SPECIFIC TUBULIN TYROSINE-LIGASE -LIKE PROTEIN PREP., ISOL., VECTOR-MEDIATED GENE TRANSFER, EXPRESSION IN HOST CELL, APPL. CANCER, REPRODUCTIVE DISORDER, TESTICULAR DISORDER, PULMONARY DISORDER, GASTROINTESTINAL DISORDER, NEURAL DISORDER, IMMUNOLOGICAL DISORDER, ARTHRITIS, ASTHMA, AIDS, SEPSIS, ACNE DIAGNOSIS, THERAPY, GENE THERAPY PROTEIN TUMOR (23, 14)

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(FILE 'HOME' ENTERED AT 12:08:31 ON 28 FEB 2006)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCPLUS, NTIS, LIFESCI' ENTERED AT 12:09:07 ON 28 FEB 2006

L1 7010 S TESTIS (W) SPECIFIC
L2 431 S TYROSINE (W)LIGASE?

L3 3 S L1 AND L2
L4 2 DUP REM L3 (1 DUPLICATE REMOVED)
L5 405 S TUBULIN (A) L2
L6 7556238 S CLON? OR EXPRESS? OR RECOMBINANT
L7 83 S L5 AND L6
L8 39 DUP REM L7 (44 DUPLICATES REMOVED)
L9 8 S L8 AND TESTIS
 E FEDER J N/AU
L10 185 S E3
 E WU S/AU
L11 3568 S E3
 E NELSON T C/AU
L12 130 S E3
L13 3853 S L10 OR L11 OR L12
L14 1 S L2 AND L13

10/6/5,659

| | L # | Hits | Search Text |
|----|-----|------------|--|
| 1 | L2 | 0 | tyrosine adj ligase.ti. |
| 2 | L1 | 107 | ligase.ti. |
| 3 | L3 | 606 | testis adj specific |
| 4 | L4 | 2 | tyrosine adj ligase? |
| 5 | L5 | 0 | l3 same ligase? |
| 6 | L6 | 3261 1 | ligase\$2 |
| 7 | L7 | 8171 70 | clon\$3 or express\$3 or recombinant |
| 8 | L8 | 1656 7 | l6 same l7 |
| 9 | L9 | 17 | l3 same l8 |
| 10 | L10 | 1697 34 | FEDER WU NELSON |
| 11 | L11 | 58 | l1 and l10 |

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| 1 | 20060202 | 74 | US 2006002473 1 A1 | Detection of nucleic acid sequence differences using coupled ligase detection and polymerase chain reactions |
| 2 | 20051222 | 119 | US 2005028281 8 A1 | Ubiquitin ligase inhibitors |
| 3 | 20051201 | 35 | US 2005026648 7 A1 | High fidelity thermostable ligase and uses thereof |
| 4 | 20051201 | 34 | US 2005026643 9 A1 | Thermostable RNA ligase from thermus phage |
| 5 | 20051020 | 69 | US 2005023332 0 A1 | DETECTION OF NUCLEIC ACID SEQUENCE DIFFERENCES USING THE LIGASE DETECTION REACTION WITH ADDRESSABLE ARRAYS |
| 6 | 20050630 | 237 | US 2005014254 3 A1 | Method of designing addressable array for detection of nucleic acid sequence differences using ligase detection reaction |
| 7 | 20050303 | 16 | US 2005004921 4 A1 | Inhibition of E3-ubiquitin ligase HAKAI for treatment of proliferative disorders |
| 8 | 20050217 | 122 | US 2005003734 6 A1 | High fidelity detection of nucleic acid differences by ligase detection reaction |
| 9 | 20041223 | 82 | US 2004025914 1 A1 | Detection of nucleic acid sequence differences using the ligase detection reaction with addressable arrays |

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| 10 | 20041216 | 70 | US 2004025362 5 A1 | Detection of nucleic acid sequence differences using the ligase detection reaction with addressable arrays |
| 11 | 20041028 | 78 | US 2004021422 4 A1 | Detection of nucleic acid sequence differences using coupled ligase detection and polymerase chain reactions |
| 12 | 20041014 | 77 | US 2004020306 1 A1 | Detection of nucleic acid sequence differences using coupled ligase detection and polymerase chain reactions |
| 13 | 20040902 | 199 | US 2004017113 1 A1 | Polynucleotides encoding a novel testis-specific tubulin tyrosine-ligase-like protein, BGS42 |
| 14 | 20040812 | 171 | US 2004015723 4 A1 | Polynucleotides encoding a novel testis-specific tubulin tyrosine-ligase-like protein, BGS42 |
| 15 | 20040422 | 52 | US 2004007697 3 A1 | Antisense modulation of ubiquitin protein ligase expression |
| 16 | 20030918 | 111 | US 2003017575 0 A1 | Detection of nucleic acid sequence differences using the ligase detection reaction with addressable arrays |
| 17 | 20030515 | 260 | US 2003009212 8 A1 | Nucleic acid encoding RNA ligase of bacteriophage RM 378 |

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| 18 | 20030501 | 262 | US 2003008279 0 A1 | RNA ligase of bacteriophage RM 378 |
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| 19 | 20030501 | 118 | US 2003008254 5 A1 | High fidelity detection of nucleic acid differences by ligase detection reaction |
| 20 | 20030213 | 82 | US 2003003201 6 A1 | Detection of nucleic acid sequence differences using coupled ligase detection and polymerase chain reactions |
| 21 | 20030130 | 78 | US 2003002218 2 A1 | Detection of nucleic acid sequence differences using the ligase detection reaction with addressable arrays |
| 22 | 20021017 | 70 | US 2002015092 1 A1 | Detection of nucleic acid sequence differences using the ligase detection reaction with addressable arrays |
| 23 | 20020411 | 56 | US 2002004208 3 A1 | Ubiquitin ligase assay |
| 24 | 20020228 | 44 | US 2002002556 9 A1 | COMPONENTS OF UBIQUITIN LIGASE COMPLEXES AND USES RELATED THERETO |
| 25 | 20020221 | 25 | US 2002002225 8 A1 | Ubiquitin ligase |
| 26 | 20050927 | 35 | US 6949370 B1 | High fidelity thermostable ligase and uses thereof |
| 27 | 20050208 | 75 | US 6852487 B1 | Detection of nucleic acid sequence differences using the ligase detection reaction with addressable arrays |
| 28 | 20041214 | 40 | US 6831208 B1 | 4-coumarate co-enzyme a ligase promoter |

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| 29 | 20041116 | 253 | US 6818425 | RNA ligase of bacteriophage RM 378 |
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| 30 | 20040928 | 77 | US 6797470 B2 | Detection of nucleic acid sequence differences using coupled ligase detection and polymerase chain reactions |
| 31 | 20040615 | 27 | US 6750057 B2 | Ubiquitin ligase |
| 32 | 20040608 | 42 | US 6747128 B2 | Components of ubiquitin ligase complexes, and uses related thereto |
| 33 | 20040525 | 46 | US 6740495 B1 | Ubiquitin ligase assay |
| 34 | 20040518 | 55 | US 6737244 B2 | Ubiquitin ligase assay |
| 35 | 20030610 | 107 | US 6576453 B2 | Thermostable DNA ligase mutants |
| 36 | 20030114 | 103 | US 6506594 B1 | Detection of nucleic acid sequence differences using the ligase detection reaction with addressable arrays |
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| 38 | 20011106 | 114 | US 6312892 B1 | High fidelity detection of nucleic acid differences by ligase detection reaction |
| 39 | 20010828 | 27 | US 6280998 B1 | Purified thermostable pyrococcus furiosus DNA ligase |
| 40 | 20010731 | 77 | US 6268148 B1 | Detection of nucleic acid sequence differences using coupled ligase detection and polymerase chain reactions |

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| 41 | 20010710 | 47 | US 6258601 B1 | Antisense modulation of ubiquitin protein ligase expression |
| 42 | 20010403 | 28 | US 6211161 B1 | UDP-N-acetylmuramoyl-l-alanine:D-glutamate ligase (MURD) of staphylococcus aureus |
| 43 | 20000425 | 50 | US 6054564 A | Thermostable ligase mediated DNA amplification system for the detection of genetic diseases |
| 44 | 20000222 | 77 | US 6027889 A | Detection of nucleic acid sequence differences using coupled ligase detection and polymerase chain reactions |
| 45 | 19991102 | 7 | US 5976806 A | DNA ligase assay |
| 46 | 19990727 | 20 | US 5929045 A | Recombinant expression of polynucleotides encoding the UDP-N-acetylmuramoylalanine:D-glutamate ligase (MurD) of Streptococcus pneumoniae |
| 47 | 19990608 | 25 | US 5910408 A | Catalytic DNA having ligase activity |
| 48 | 19981103 | 52 | US 5830711 A | Thermostable ligase mediated DNA amplification system for the detection of genetic diseases |
| 49 | 19980811 | 24 | US 5792607 A | Method and kits for amplifying target nucleic acids applicable to both polymerase and ligase chain reactions |

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| 50 | 19980609 | 25 | US 5763256 A | Serine protease variants having peptide ligase activity |
| 51 | 19980407 | 31 | US 5736512 A | Serine protease variants having peptide ligase activity |
| 52 | 19971223 | 27 | US 5700672 A | Purified thermostable pyrococcus furiosus DNA ligase |
| 53 | 19970513 | 33 | US 5629173 A | Methods of use of serine protease variants having peptide ligase activity |
| 54 | 19960702 | 30 | US 5532146 A | Method for rendering ligase-based amplification products unamplifiable |
| 55 | 19960409 | 32 | US 5506137 A | Purified thermostable Pyrococcus furiosus DNA ligase |
| 56 | 19960227 | 49 | US 5494810 A | Thermostable ligase-mediated DNA amplifications system for the detection of genetic disease |
| 57 | 19950404 | 27 | US 5403737 A | Serine protease variants having peptide ligase activity |
| 58 | 19870428 | 38 | US 4661450 A | Molecular cloning of RNA using RNA ligase and synthetic oligonucleotides |

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| 1 | 20040902 | 199 | US 2004017113 1 A1 | Polynucleotides encoding a novel testis-specific tubulin tyrosine- ligase-like protein, BGS42 |
| 2 | 20040812 | 171 | US 2004015723 4 A1 | Polynucleotides encoding a novel testis-specific tubulin tyrosine- ligase-like protein, BGS42 |

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| 1 | 20051117 | 358 | US 2005025511 4 A1 | Methods and diagnosis for the treatment of preeclampsia |
| 2 | 20050922 | 103 | US 2005020850 0 A1 | Signatures of ER status in breast cancer |
| 3 | 20050818 | 212 | US 2005018137 5 A1 | Novel methods of diagnosis of metastatic cancer, compositions and methods of screening for modulators of metastatic cancer |
| 4 | 20050721 | 15 | US 2005015875 6 A1 | Identification of a gene expression profile that differentiates ischemic and nonischemic cardiomyopathy |
| 5 | 20040422 | 253 | US 2004007695 5 A1 | Methods of diagnosis of bladder cancer, compositions and methods of screening for modulators of bladder cancer |
| 6 | 20040325 | 135 | US 2004005834 0 A1 | Diagnosis and prognosis of breast cancer patients |
| 7 | 20040226 | 259 | US 2004003820 7 A1 | Gene expression in bladder tumors |
| 8 | 20040129 | 111 | US 2004001851 3 A1 | Classification and prognosis prediction of acute lymphoblastic leukemia by gene expression profiling |
| 9 | 20040108 | 165 | US 2004000556 0 A1 | Novel full-length cDNA |
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| 11 | 20031211 | 206 | US 2003022857 0 A1 | Methods of diagnosis of Hepatitis C infection, compositions and methods of screening for modulators of Hepatitis C infection |
| 12 | 20031204 | 104 | US 2003022437 4 A1 | Diagnosis and prognosis of breast cancer patients |
| 13 | 20021024 | 753 | US 2002015511 9 A1 | Isolation and use of fetal urogenital sinus expressed sequences |
| 14 | 20020124 | 57 | US 2002000973 0 A1 | Human stress array |
| 15 | 20051227 | 118 | US 6979557 B2 | Full-length cDNA |
| 16 | 20040316 | 434 | US 6706867 B1 | DNA array sequence selection |
| 17 | 20020101 | 227 | US 6335170 B1 | Gene expression in bladder tumors |